The Southern Surgeon

Medical College of Alabama Number

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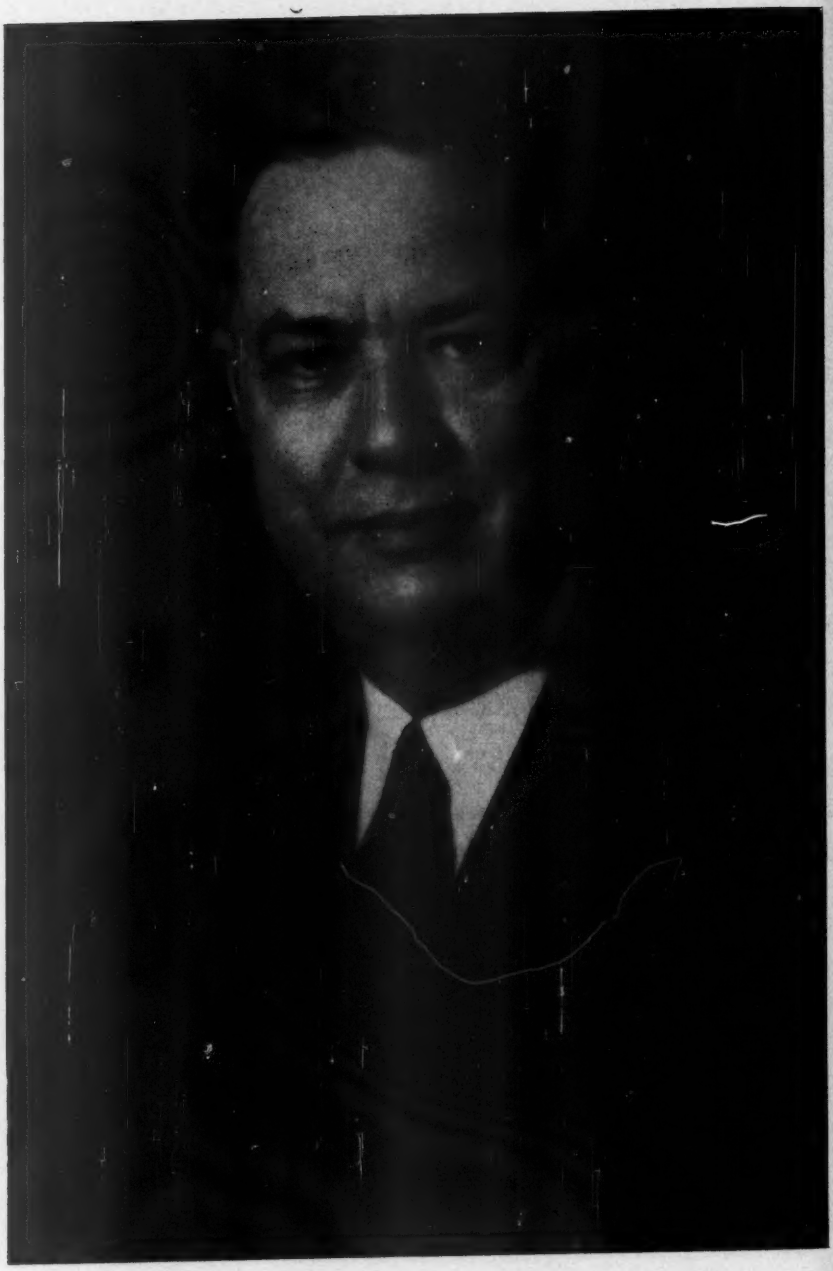

DR. E. L. HENDERSON
President, Southeastern Surgical Congress, 1947

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TO THE PROFESSION:

Since World War II is now officially behind us we can look forward to an unrestricted meeting of The Southeastern Surgical Congress. While it was not possible for us to hold meetings from 1942 to 1946, a more or less restricted meeting was held in Memphis in 1946. Due to the lack of adequate hotel accommodations, our meeting was more or less curtailed. We are hoping to have a sufficient number of hotel rooms in Louisville for the meeting to be held at the Brown Hotel, March 10, 11, 12.

The Southeastern Surgical Congress is composed of leading surgeons from the eleven states making up the southeastern section of the United States. During the past years the programs have been outstanding, the speakers being chosen from the best teachers in the United States. In looking over the program for the coming Assembly, in March, 1947, one is impressed with its outstanding features, and we feel that the three days' condensed program offers to the profession the greatest Postgraduate Course in Surgery that can be obtained.

Your officers anticipate with pleasure the coming Assembly and extend a most cordial invitation to the members of the profession to attend the meetings.

E. L. HENDERSON, M.D.,
President.

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MALIGNANT MELANOMA IN THE NEGRO

With Report of Six Cases

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and
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MOST of the articles dealing with malignant melanoma note the relative rarity of this disease in the North American negro. No satisfactory explanation has been given as to why benign and malignant pigmented tumors occur infrequently in tissues which normally have considerable pigment. As far back as 1896, Matas[1] pointed out the uncommon occurrence of malignant melanoma in the negro and proposed the theory that in highly pigmented people the physiologic function of pigment formation was under better biologic control and, therefore, less liable to unrestrained growth. A corollary has been observed in that malignant melanoma occur more often in light colored horses than in dark horses.

A survey of the literature reveals that a total of 73 cases of malignant melanoma in the North American negro have been mentioned or described.

Gilchrist's account (1899) of a malignant melanoma starting on the sole of the foot is the earliest case recorded.[2,3] This patient gave a history of a small elevated pigmented area with rapid growth after being shaved with a razor. Not until 1920 did the next article appear, when Hazen[4] published a report of a male negro who developed a malignant melanoma six months after a nail puncture wound through a mole on the foot.

A critical analysis of this subject was published by Sutton and Mallia (1923).[5] They presented a detailed case report of a malignant melanoma starting on the foot of a negress. This patient gave a history of a dog bite nine years before the development of the tumor. Menage[6] listed 5 cases from the records of the Charity Hospital of Louisiana in New Orleans. In three instances the tumor started on the foot, once on the scalp and once on the thumb. Carmichael[7] mentioned an additional case which started on the ankle.

Two cases were reported by Bauer (1927).[8] In the first case, the lesion began on the great toe of a negro male with a history of trauma three years prior to the appearance of the tumor. The

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From the University Tumor Clinic, Medical College of Alabama.

second case was a subungual melanoma in the thumb of a negress, aged 23. This patient had a history of injury fifteen months before the onset of the malignant growth.

Pack[9] reported 3 cases located on the plantar surface of the foot, hand, and mucous membrane of the superior alveolus respectively. The primary lesion in the mouth is the first such case reported in a negro. A primary malignant melanoma on the right eye with generalized metastases was reported by Knighton[10] in 1931. This lesion occurred in a colored male, aged 33. Dickson and Jarmon[11] (1932) reported a case of subungual melanoma in a negress, aged 73, with a twenty year history of a pigmented area beneath the nail of a finger.

The literature was reviewed by Bishop[12] (1932) and he reported 9 additional cases. Of these 4 occurred on the foot, 2 on the thigh, one on the upper lip, supra-orbital area, and eye respectively. Two of the above cases were from a group of 5 melanomata in the negro seen at Grady Municipal Hospital in Atlanta. The remaining 7 cases are from the records of the Steiner Clinic in Atlanta. A total of 12 cases are mentioned in this article.

In a series of 50 cases of malignant melanoma seen at the Philadelphia General Hospital, Butterworth and Klauder[13] (1934) reported the presence of this disease in 6 negroes, one of whom was a mulatto. They reviewed 598 cases of malignant melanoma and found that they were about equally divided between the sexes. Slightly more than one half of the primary tumors were on the foot. Hewer[14] (1935) reviewed the tumor material from the surgical pathologic laboratory, Johns Hopkins University, and in 60,000 specimens in the past forty years, he found 343 melanomata in the white race and 10 in negroes. He notes that malignant melanoma is about equally common on the soles of the feet in both white and colored individuals. The latter finding lessens the importance of the belief that malignant melanoma in the negro tend to develop in areas of partial pigmentation. Hewer also reported a series of 47 cases from natives of the Sudan and in this series of Sudanese cases, 59.5 per cent arose on the foot. The incidence of occurrence on the foot is only slightly higher than that given for the white race (52 per cent).[13] This fact would tend to discount the suggestion that the rarity in the North American negro may be due to the fact that he wears shoes.

Affleck[15] (1936) reported 2 cases. Herold[16] (1936) reported a primary lesion arising on the hand. Three cases were reported by Quinland[17] in 1936. In one instance the primary site could not be

determined because of the generalized metastases, one lesion starting on a finger and the third case had a primary melanoma in the nostril. The latter case is the first recorded malignant melanoma in the negro with the primary site in the nose. The 3 cases reported by Quinland were from a twelve year collection of pathologic material at the George W. Hubbard Hospital, Meharry Medical College, Nashville, Tennessee. The nasal tumor occurred in a negress, aged 44. The nostril was occluded one week after the growth was first noted and generalized metastases were present one year later. The microscopic diagnosis was melanosarcoma.

An unusual case of a primary melanoma in the scalp with metastatic involvement of the heart was published by Morgagues[18] (1937). He reviewed the literature and found 23 cases of metastatic melanoma in the heart. Morgagues added 4 cases, one of which was a negress, aged 39, mentioned above.

Baxter[19] (1939) reported a single case of melanoma arising in the mouth of a negro male, aged 51. The primary lesion originated on the mucous membrane above the upper left incisor teeth and is the second such case to be published. Seven cases of malignant melanoma in the negro were reported by Pack and Adair[20] (1939). One of these was subungual in location, but the primary sites of the others were not mentioned. The subungual lesion was in a male, aged 59.

Anderson[21] (1941) reviewed the previous reports and added 10 cases which were located as follows: foot 5, subungual 3, eye and leg each one. Six of the cases had a history of previous trauma. These 10 cases were obtained from a group of 14,000 surgical specimens at the John Gaston Hospital in Memphis. The same specimens also provided a series of 12 cases in the white race with approximately 78 per cent of the specimens from negroes.

Kaplan[22] (1942) stated that in seventeen years at the New York City Cancer Institute only 40 melanomata were seen and only 4 of these were in negroes. The location of the primary lesions were not mentioned.

Malignant Melanoma in the Nose

Ringertz,[23] in a detailed survey of the malignant tumors arising in the nose, paranasal cavities and maxilla, feels that malignant melanomata in this area probably arise from melanoblasts of mesenchymal origin. He states that about 50 cases of malignant melanoma of the nose and paranasal regions have been reported. In considering primary lesions in this area, secondarily invading neo-

plasms from the palate, orbit and nasopharynx must be ruled out. Ringertz mentions 2 cases of primary melanoma of the skin with metastases in the nasal cavity. He reports 6 cases and summarizes the findings from 36 previously reported cases. In no instance did the tumor arise in the vestibule. Malignant melanoma in the nose often grow rather slowly and metastasize late. The symptoms are mainly those of mechanical obstruction and bleeding. Pain is seldom reported. Ringertz makes no mention of the occurrence of malignant melanoma in the nose or paranasal region of the negro. Kaplan[22] (1942) reviewed 58 cases of malignant melanoma arising in the nose and added 2 cases to make a total of 60 reported cases. In a period of seventeen years at Bellevue and Lennox Hill Hospitals, he did not see a case of malignant melanoma in the negro. The only recorded instance of a primary malignant melanoma arising in the nose of a negro was reported by Quinland[17] in 1936. Including the case reported below, a survey of the literature reveals a total of 62 cases of malignant melanoma of the nose, 2 of which are negroes.

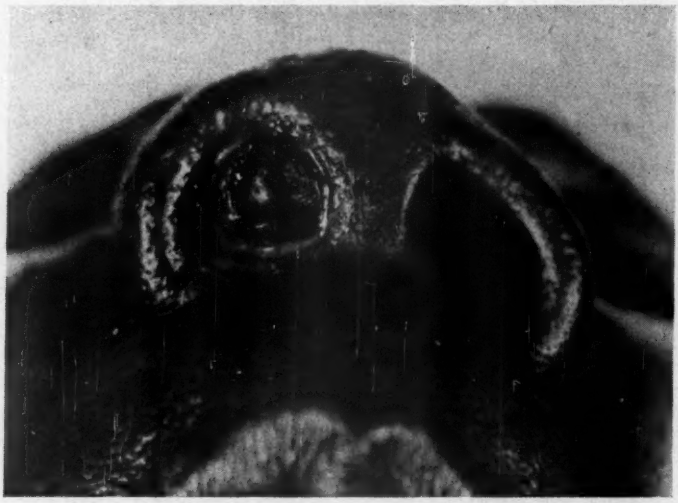

Fig. 1. Case 1, colored female, aged 66, with malignant melanoma arising from lateral wall of right nostril.

CASE 1: E. M., colored female, aged 66, gave a history of bumping her left breast against a door in July, 1939, and six months later developed a bloody discharge from the left nipple. Two weeks after the onset of the bleeding, the patient noticed a lump beneath the left nipple and on Feb. 3, 1940, reported to the out-patient clinic. A microscopic diagnosis of scirrhous

carcinoma was made and a radical mastectomy performed in February, 1940. A series of postoperative deep x-ray treatments (factors unknown) were given and the patient apparently remained free of active disease for eighteen months. Cutaneous metastases and local recurrences in the scar then appeared and a second course of x-ray treatments (factors unknown) were given followed by some regression of the tumor. Further recurrences developed and these were excised in June, 1943, March, 1944, and March, 1945.

The patient first noticed a mass in the right nostril in December, 1945. This rapidly increased in size and occluded the nares. In February, 1946, a dark bluish polypoid mass was removed from the lateral wall of the right nostril with a subsequent diagnosis of malignant melanoma. The mass recurred in July, and in August of this year (fig. 1) she again began having symptoms of obstruction and bleeding. A series of deep x-ray treatments were delivered to the nose through a 5 x 5 cm. port from Sept. 25 through Oct. 8, 1946, using the following factors: 220 kv.; 15 MA; 50 cm. STD; ½ mm. Cu. and 1 mm. Al. added filtration; hvl 0.9 mm. cu.; 48 r/min; 300 r, air dose, daily for a total of 3000 r.

The irradiation produced a slight regression of the tumor and a cessation of the bleeding. Extensive local recurrences are present in the operative scars of the left anterior chest wall and a number of cutaneous metastases have developed in the surrounding skin. At the present time, there is no evidence of regional metastases from the melanoma of the nose or distant metastases from the carcinoma of the breast. This patient presents the interesting findings of a primary carcinoma of the breast and a primary malignant melanoma of the right nostril.

Malignant Melanoma of the Mouth

Baxter[24] (1941) reviewed the subject of malignant melanoma of the mouth and summarized a total of 54 reported cases which did not include lesions of the tonsil and pharynx. Of these, 48 were in the white race, 4 in orientals and 2 in negroes. In 36 cases, it originated on the hard or soft palate, in 15 cases on the alveolar process of the maxilla, once on the tongue, once on the mandible and once on the lower lip and cheek. In 93 per cent of the cases, the primary lesion arose on the palate or alveolar process of the maxilla. Where the sex was mentioned, 35 were in males and 14 in females. Baxter reported an additional case in a white male with the primary site on the alveolar process of the maxilla to make a total of 55 cases of oral malignant melanoma. Direct extension from the nasal or paranasal regions and metastatic involvement must be ruled out. Simpson and Graham[25] review 4 cases of metastatic melanoma of the tonsils. Bleeding, pain, and difficulty in eating are the most common symptoms of oral malignant melanoma.

Including the case reported below, an analysis of the literature reveals the presence of 56 instances of primary malignant melanoma in the mouth, 3 of which are negroes.

Case 2. C. C., colored female, aged 43, was admitted to the hospital with

a diagnosis of ulcerative stomatitis. Three weeks prior to admission this patient had first noticed a "knot about the size of a pea" on her right lower gum at about the level of R-11. This caused the patient some slight discomfort and she consulted a druggist who gave her a white powder to apply

Fig. 2. Case 2, colored female, aged 43, with massive growth of a primary lesion starting on the right lower gum.

locally. She stated that the medicine gave her some relief but that "the more she rubbed, the more it grew." At the time of admission, it involved a 4 cm. length of the gum and extended into the gingival-buccal sulcus and into the sublingual area to produce some protrusion of the lower lip and elevation of the tongue. The patient stated that she thought that the lump was caused by "dipping snuff" and gave a history of using one box of snuff weekly for many years. The tumor had a dirty, ulcerated and necrotic appearance and was quite dark in color. A biopsy was taken and the patient placed on mouth washes and penicillin. The tissue was reported as malignant melanoma with only a small amount of melanin present. The tumor was composed of sheets of large, round cells closely packed and with very little intercellular tissue. Physical examination and x-ray of the chest revealed no evidence of metastatic involvement. X-ray studies showed an irregular area of destruction in the region of the symphysis. A series of deep x-ray treatments to the pituitary

gland were given from March 28 through April 10, 1946, using the following factors: 200 kv.; 20 MA; 50 cm. STD; ½ mm. Cu. and 1 mm. Al. added filtration; 54 r/min; 100 r, air dose, daily alternating right and left 7 x 7 cm. lateral ports for a total of 600 r, air dose, to each port. The mass continued to increase in size each day during the course of the treatments (fig. 2) and a radical resection was done on April 12. At operation the lesion was found to involve the entire floor of the mouth anteriorly, with extension to the right cheek and lower lip. The mass measured 9 x 7 x 5 cm. The entire anterior one half of the floor of the mouth, mandible, and lower lip were removed as one specimen. Radical dissection of the lymph glands in the submental and submaxillary areas was performed after removal of the primary lesion. At completion of the operation, the patient appeared to be in excellent condition, but suddenly expired four hours later. Permission for postmortem examination could not be obtained. The extent to which the snuff might have acted as a stimulating factor in the development of this lesion is uncertain but must be considered.

Malignant Melanoma of the Intestine

Malignant melanoma of the intestine is an uncommon condition in the negro. The authors were unable to find a single reported case. Ewing[26] states that diffuse melanosis of the colon is not infrequent in elderly individuals but that malignant melanoma is almost exclusively confined to the rectum. A single case of malignant melanoma arising in the rectum of a negro is reported through the courtesy of Dr. George Goodall and is described below.

Case 3. W. C., colored male, aged 61, was admitted to the hospital on March 5, 1946, with the complaint of dark stools and frequency of bowel movements. The patient gave history of feeling well until January, 1946, when he developed "piles" which were characterized by occasional bright red blood in the stools and painful defecation. Physical examination revealed two small subcutaneous nodules beneath the skin of the right anterior chest wall. Rectal examination revealed an irregular, nodular, ulcerated, fixed and nontender mass on the anterior wall of the rectum just within the anal orifice. Proctoscopic examination revealed a dark fungating mass on the left anterior rectal wall. A biopsy was obtained and microscopic examination disclosed the presence of a malignant melanoma with considerable intracellular deposits of melanin. X-ray examination of the chest was negative for metastases. A colostomy was done on March 15 and numerous black nodules were present on the peritoneum and in the omentum. The rectal mass was fixed in position. Tissue removed from the peritoneum, omentum and subcutaneous nodules all showed malignant melanoma with abundant pigment in the cells. The patient expired on March 24 and permission for autopsy could not be obtained.

Three additional cases of malignant melanoma in the negro were obtained from the files of the Jefferson-Hillman Hospital and are described below.

Case 4. P. T., colored female, aged 45, had a small growth removed from the skin of the interscapular area on July 10, 1936, with a provisional diagnosis of keloid or lipoma. The pathologic diagnosis was melanosarcoma. In

August, 1942, she was admitted to the hospital complaining of several large nodules in each axilla and of shortness of breath. Physical examination revealed ascites and edema of the right arm in addition to the large masses in the axillae. A urine specimen was positive for melanin. The patient had a rapid downhill course and died on Aug. 28, 1942. A request for autopsy was refused.

CASE 5. J. M., colored male, aged 58, was seen on Sept. 22, 1943, complaining of a "sore" on the plantar surface of the right great toe which had been present for nine months. There was no history of trauma. Physical examination revealed a darkly pigmented and edematous foot with a small gangrenous area on the plantar surface of the right great toe. The heavy pigmentation extended up to the ankle. On Oct. 2, 1943, the right great toe was amputated at the metatarsophalangeal joint and a pathologic report of malignant melanoma was given. A right inguinal dissection and amputation of the leg at the junction of the upper and middle thirds were on Oct. 18, 1943. The inguinal lymph glands contained metastatic tumor. The cells showed marked irregularity and considerable intracellular melanin. X-ray examination of the chest was negative for metastases. The patient was discharged on Nov. 25, 1943. He was re-admitted to the hospital on Jan. 19, 1946, complaining of abdominal pain for one month and a left-sided paralysis present for one day. The patient soon succumbed. Postmortem examination was refused. The provisional diagnosis at death was intracranial hemorrhage or melanosis.

CASE 6. D. H., colored male, aged 65, with complaints of pain in the left leg and loss of weight, was admitted on March 3, and expired on March 21, 1943. Physical examination was negative except for several enlarged lymph glands in the left inguinal region. One of the glands was removed and a diagnosis of malignant melanoma established. Autopsy was refused and the site of the primary lesion was unknown.

DISCUSSION

Malignant melanomas show a widely diversified histologic appearance and may simulate sarcoma, carcinoma, endothelioma or lymphosarcoma. The term melanocarcinoma is usually applied to these lesions which show a preponderance of epithelioid cells and the term melanosarcoma is often used when the cells are predominantly spindle-shaped. These lesions have been variously classified as melanocarcinoma, melanosarcoma, nevocarcinoma, nevosarcoma, melano-epithelioma, pigmented cancer and melanblastoma. There is no demonstrable variation in response to treatment or clinical course of the disease among these various sub-groups. Since some of these tumors may have features compatible with several of the above types, the terms malignant melanoma or melanoblastoma appear adequately to cover all of the many morphologic variations. Malignant melanoma in the negro is similar in histologic appearance to the lesions seen in white individuals and there is no apparent difference in the relative malignancy. The microscopic pictures of the primary and metastatic lesions are frequently dissimilar.

Questions concerning the origin of malignant melanoma have produced much controversy and the problem is still unsettled. Masson[26] has presented strong evidence that melanomas arise from the end apparatus of the sensory nerve and his theory of origin is the one generally accepted by most investigators. The various sources of origin that have been proposed[27] are (1) the epithelium, (2) perithelium or endothelium of blood vessels, (3) end apparatus of the sensory nerves and (4) the melanoblast. The melanoblasts are cells capable of changing the chromogenic material of the blood into melanin. These cells are thought to contain an oxidizing ferment which acts on the colorless chromogenic material in the blood plasma.[28] Spencer[3] has made the interesting observation of the similarity of the physiologic effects of adrenalin and melanin. Sutton and Mallia[5] suggested that the suprarenals might be associated with pathologic pigmentation.

The amount of pigmentation present is no indication of the degree of malignancy, although it is felt that considerable amounts of melanin mean a high degree of differentiation. This is of little clinical importance since varying amounts of pigment may exist in the same tumor.

The incidence of this disease in the white race as compared with the negro has been variously estimated as 3 or 4 to 1.[14,21] The frequency is about equally divided between male and female.

The role of trauma as an activating agent has been stressed by many writers. Malignant melanoma is one type of malignancy in which many cases have an indisputable relationship with trauma. Cholnoky[29] mentions the injudicious use of the electric needle as an activating agent in 4.3 per cent of his series of 117 cases and quotes a figure of 10 per cent reported by Adair. Butterworth and Klauder[13] feel that in many cases the association of trauma with the onset of the growth has been so remote as to raise considerable doubt that there has been any direct relationship.

A satisfactory clinical classification has been proposed by Dawson.[30] He divided the disease into four clinical stages: (1) nevus showing increased pigmentation or increase in size, (2) melanoma with well developed local lesion, (3) melanoma with regional metastases and (4) generalized melanoma (melanosis).

It is not within the scope of this paper to make a detailed discussion of the various phases of treatment. The reader is referred to the many articles dealing with this specific problem. In general, when the lesion is clinically classified as stage 1, 2 or 3, the treatment of choice is that of wide surgical excision of the primary tumor. Radical dissection of the regional lymph glands must be

given serious consideration even though metastases are not evident or expected. Reports of favorable results with various forms of irradiation therapy are so infrequent that its use is not ordinarily advised. Attention is called to the use of pituitary irradiation[31] in an attempt to control the growth and extension of the disease. The existence of a melanophore producing hormone in the human hypophysis has been described.[32,33] One of us (AEI) has had many instances of favorable response to this type of therapy, particularly in the treatment of diffuse skeletal involvement from cancer of the breast and prostate.

Summary and Conclusions

Malignant melanoma in the negro probably occurs more often than is realized or than is evidenced by the scarcity of reports in the literature.

The relative scarcity of malignant melanoma in the negro is possibly best explained on the basis of better physiologic control of pigment formation.

There are no findings to support the belief that malignant melanoma in the negro is more apt to develop in areas of partial pigmentation.

The origin of malignant melanoma is still unsettled but the authors favor the supposition that these tumors arise from melanoblasts, either from a separate cell entity or from melanoblasts of epithelial and mesenchymal origin.

The ratio of incidence in white and colored individuals is estimated as 3 or 4:1.

A total of 73 cases of malignant melanoma in the negro have been recorded and these with the 6 cases presented by the authors make a grand total of 79 cases.

Six cases of malignant melanoma in the negro are reported. One of these is the second instance of a primary lesion developing in the nose, one is the third reported case of a malignant melanoma occurring in the mouth and another is the first instance of a primary lesion in the rectum. In two other cases the primary sites were the plantar surface of the great toe and the skin of the back. In one patient it was impossible to determine the site of the primary lesion.

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UTERINE BLEEDING: PUBERTY, MATURITY, POST CLIMACTERIC

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Of the various problems that confront the gynecologist, one of the most complicated and perplexing is abnormal uterine bleeding. To begin with, uterine bleeding is not a disease entity but a symptom; and the diagnosis of it should be approached from that angle. Too often hemostasis is the goal and no attempt is made to diagnose the primary cause.

Nothing is more important in diagnosis than a thorough history and a general physical examination. The data thus obtained will furnish a basis for selecting further aids in diagnosis such as the metabolism test, vaginal cytology smears, endometrial biopsy, curettage or if necessary some of the more complex hormonal studies.

NORMAL MENSTRUATION

As a background for discussion of abnormal uterine bleeding, a brief resume of the possible causes of normal menstruation will be reviewed. The "growth wave theory" of menstruation is one of the most plausible explanations for both normal and abnormal uterine bleeding.[1] Due to stimulation of the ovaries by the pituitary gland, cyclic waves of estrogen are secreted which cause growth and regression of the endometrium. There appears to be a certain estrogen blood level at which bleeding usually occurs, and above that blood level bleeding will cease. When the estrogen blood level drops to the bleeding level, the endometrial vascular apparatus is affected. The spiral arterioles in the endometrium undergo spasm with resultant anoxemia and focal necrosis of the upper two-thirds of the endometrium. When the vasoconstriction of the various arterioles relaxes, bleeding results. However, the arterioles will continue to bleed off and on until a new estrogen wave causes regrowth of the endometrium.[2]

Progestin is thought to contribute only to the secretory function of the endometrial glands and has very little to do with uterine bleeding.[3]

ANOVULATORY BLEEDING

It is now accepted that anovulatory menstrual cycles occur in woman; and it can be proved by finding a proliferative endometrium

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when an endometrial biopsy has been taken during the first few hours of menstruation. This is usually associated with a disturbed relationship between the ovary and the pituitary. The resultant estrogen formation is often not cyclic and may drop to or near bleeding levels which may cause frequent and perhaps profuse bleeding. If the estrogen level should remain high over a long period of time the endometrium becomes hyperplastic and cystic as noted in the hyperplasias of the endometrium which tend to bleed on any drop of the blood estrogen level.[4]

Functional bleeding is more frequent near the menarche and climacteric, at which time the relationship between the pituitary and the ovary is unstable.

Adolescent Bleeding

In the adolescent girl sexual development is a gradual process. The ovary is stimulated to produce increasing amounts of estrogen which causes development of the secondary sex characteristics, including development of the internal pelvic organs, with the menarche occurring a year or more later. Actual ovulation, and therefore full sexual maturity, usually does not take place for several more years. During that time the ovary has anovulatory cycles with varying amounts of estrogen production which may at times subject the girl to profuse and prolonged bleeding episodes.[5]

A close relationship between the various endocrine glands has been noted, and dysfunction of one causes abnormal function in the other. Such is the case in hypothyroidism which may be the underlying cause of scanty and infrequent bleeding or may cause profuse and frequent bleeding.

Uterine bleeding of this type can be controlled by large doses of estrogen which may be continued for varying lengths of time until the blood loss has been compensated for and the general level of health elevated.[6] Where thyroid is indicated, tolerance doses should be given.

Irregular Bleeding of Maturity

In the mature woman, functional bleeding assumes a more minor role with organic causes of uterine bleeding coming to the fore.

Complications of pregnancy are the most common causes of uterine bleeding in this age group. Threatened abortion and retained placental tissue are most common, but mention should be made of placenta previa, hydatidiform mole, premature separation of placenta and the very occasional case of chorio-epithelioma as possible

causes of bleeding. Curettage and microscopic examination of the tissue obtained will usually yield a correct diagnosis.

Malignant tumors of the uterus and ovaries cause most anxiety and furnish the principal reason for a meticulous search to rule out such conditions. Biopsy of the cervix and curettage of the fundus should indict or clear the uterus. However, the functioning tumors of the ovary, such as the granulosa and the thecal cell tumors, of which a certain percentage is malignant, are most difficult to diagnose during active menstrual life unless a definite tumor mass is found or an abdominal operation is performed.[7]

Benign tumors, as the submucous and intramural fibromata and endometrial polyps, are very common causes of uterine bleeding. There has been much speculation lately as to whether bleeding from these conditions may not be attributed to functional uterine bleeding. The endometrium overlying the fibromata usually has a poor blood supply and for that reason may not receive the proper amount of blood-borne hormones, with resulting irregularities of bleeding from a poorly stimulated endometrium.

The polyp may be formed by a localized overgrowth of the basalis portion of the endometrium which is only stimulated by estrogen and not by progestin, and is only slightly affected by the lowering of the estrogenic blood titre to the bleeding level. When bleeding does occur it may be profuse or scant; and the tissue loss is minimal with the bulk of the polyp remaining. Occasionally the polyp reacts to progestin causing a secretory endometrium.

Endometrial hyperplasia, as noted earlier in this paper, is probably caused by the continued elaboration of estrogen over a long period of time with very little cyclic regulation.[4] This occurs during an anovulatory cycle in which pituitary stimulation is inadequate to cause ovulation. Then estrogen alone is produced by the ovary, often reaching levels low enough to allow occasional bleeding but for the most part causing a continued growth of the endometrium with cystic dilation of the glands.[8] Curettage and careful microscopic examination of the tissue by a competent pathologist are indicated.

Endometrial biopsy is invaluable as an office procedure in the diagnosis of functional uterine bleeding if taken during the first few hours of menstruation. In all women over 30 years of age that have excessive or prolonged bleeding, a curettage and careful microscopic examination by a pathologist of the tissue obtained, are important to rule out any malignancy. Curettage will also furnish temporary hemostasis which will allow time for the blood levels of an anemic patient to be improved.

Functional bleeding can be controlled immediately by large doses of estrogenic substances. If given intramuscularly and in large doses, the effect is dramatic with the bleeding being quickly checked. In the orally active estrogenic substances, the effect is not so quickly noted but good results are usually obtained. The oral forms are

SUMMARY OF 107 CASES

TABLE 1

Number of Biopsies	Per Cent of Total Biopsies	
35.5	95	Proliferative Phase, Late and Early
35.5	95	Secretory Phase, Late and Early
10.4	28	Hyperplasia of Endometrium
.74	2	Glandular Hyperplasia
.74	2	Polypoid Hyperplasia
1.08	3	Endometrial Glandular Dysplasia
.3	1	Cystic Glandular Dysplasia
5.5	15	Placental Tissue
2.8	3	Malignant Adenoma
8.6	23	Atrophic Endometrium

In this study there were 75 white and 32 colored patients and all came in primarily for irregular bleeding. There were 267 biopsies ranging from 1 to 24 biopsies per patient, or an average of 2.4. There were 15 cases, or 14 per cent, in which we found placental tissue present, but many of these patients gave no history of recent pregnancies. There were 3 instances of malignancy, or 2.8 per cent of the 107 cases. The ages of these were 26, 51 and 59 years. The youngest patient was 14 and the oldest 69 years. There was one granulosa-cell tumor in the group.

much easier to take over a long period of time and are much less expensive than the intramuscular preparations.[8]

In women of the childbearing age, treatment should be as conservative in character as possible with nothing done to impair fertility.

Endometrial biopsies are becoming more and more frequently used as they show an ever widening field of usefulness, not only in classifying bleeding cases but in revealing variations in ovarion activity in sterility studies. While such biopsies are never performed where malignancy is remotely suspected, cancer may be discovered incidentally, as was encountered in 3 cases by the writer.[9]

Bleeding During the Climacteric

In the climacteric group, the problem of functional bleeding again becomes important as various types of irregularities of menstruation are of frequent occurrence. The ovary begins to fail in its response to the gonadotropic stimulus even though the pituitary puts out a greatly increased amount of gonadotropins. This lack of response results in anovulatory cycles. The menstrual periods are often irregular with excessive and prolonged bleeding.[10]

In the climacteric, the problem of malignancy is more important than functional bleeding. In thoroughly investigated cases, 30 to 50 per cent of uterine bleeding after the menopause is due to cancer. Therefore, a responsibility is placed upon the physician to make a careful examination of the cervix, fundus and ovaries for any possible malignancies. Suspected lesions of the cervix should be biopsied. In other unexplained bleeding, the fundus and cervix should be thoroughly curetted and the material studied. No discussion is complete without the warning of the gravity of intermenstrual bleeding, which, while frequently of an innocent origin, is a favorite concomitant of cancer.

Occasionally post-climacteric bleeding will come from endometrial hyperplasia or an endometrial polyp which is found on curettage, showing that low levels of estrogen are still being produced somewhere in the body. Bleeding that comes from a fairly well developed endometrium after the climacteric is suggestive of a granulosa cell tumor of the ovary, especially if an unexplained mass is felt in either adnexal region.

Summary

Normal menstrual bleeding, the irregular flow of adolescence, the menopause and the problem of malignancy have been discussed.

The importance of early and correct diagnosis is stressed. This is especially needed in women over 30 years of age where malignancy may be suspected. Endometrial biopsy is of great value in the diagnosis and treatment of functional uterine bleeding; but in suspected malignancy of the fundus a thorough curettage is imperative.

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PRIMARY NEOPLASMS OF THE TRACHEA

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IN daily clinical experience, as well as in a review of the literature, one notes a very definite increase in the incidence of neoplasms of the bronchus and the trachea. Whether this increase is due to the more widespread, skillful use of the bronchoscope, or whether the increase is an actuality, is debatable. Irrespective of the increase in tracheal tumors this disease is still sufficiently rare to warrant reporting cases when they are found.

Although the total number of primary tracheal tumors reported remains small, there seems to be a rather widespread variation in their histologic structure. Krompecher[1] has given us a splendid concept of tumors arising from respiratory epithelium. Abnormal growth of the cells composing the undifferentiated basal layer of this pseudostratified epithelium has the potentiality of producing columnar, squamous or glandular epithelium which may result in various forms of neoplasms.

INCIDENCE

In a review of the world's literature on this subject, D'Aunoy and Zoeller[2] found 351 cases reported. Of this number, 27 were undetermined histologically. The remainder, however, were definitely determined histologically and this list contained fibroma, papilloma, lipoma, chondroma, adenoma, lymphoma, intratracheal goiter, angioma, cylindroma, sarcoma, carcinoma, and endothelioma. This great variation in the histologic structure of tracheal neoplasms obviously indicates that there will be a similar variation in the rapidity of growth in individual tumors, which is thoroughly substantiated by case reports. Fraenkel[3] found 7 cases of primary carcinoma of the trachea in 5,063 necropsies. Culp[4] found one case of squamous cell carcinoma of the trachea in 9,000 autopsies at the Pathological Institute of McGill University, and one case of squamous cell carcinoma of the trachea in 12,700 autopsies at the Montreal General Hospital. Figi[5] found 5 cases of carcinoma of the trachea in Mayo Clinic patients from 1918 to 1930. The author has found 6 cases of tracheal neoplasms in 20,433 patients seen in private practice from Aug. 1, 1940, until the present time (Oct. 4, 1946). Five of these cases have been reported previously.[6] Microphotographs of three of these specimens are shown in Figures 3,

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4a, 4b, 5a and 5b. Included in this paper is a new case to be reported. The author together with Dr. Broyles has seen one other case which was reported in 1940.[7]

Signs and Symptoms

The cardinal signs and symptoms of neoplasm of the trachea, in the authors' observation, are cough, dyspnea and hemoptysis. A patient suffering from this disease may first note a tickling sensation in the trachea which may occur only when the patient lies down. This may be aggravated by moving from side to side and produce paroxysms of coughing. This annoying sensation gradually grows worse until it becomes practically intolerable. Dyspnea may be noted at first only upon exertion, but will gradually become increasingly severe until the patient is completely incapacitated for lack of breath. This distressing symptom is usually noted on both inspiration and expiration, and may be influenced considerably by a change in position. Two of our patients reached a point where breathing was impossible except when lying on the back with the head slightly elevated. Any acute upper respiratory infection will cause the dyspnea to be considerably increased. The distressing cough and dyspnea frequently result in an incorrect clinical diagnosis of bronchial asthma. Three of our patients had been treated several months for asthma prior to bronchoscopic examination, which revealed the true nature of the disease. Hemoptysis was what caused one of our patients to seek bronchoscopic consultation. In the onset of the disease, there may be only slight blood streaking of the sputum, but as cough and exertion increase, first old clots and then active hemorrhage may result. This may eventually result in a fatal hemorrhage.

Course of the Disease

As the growth increases in size, cyanosis may develop due to increasing obstruction of the tracheal lumen. Hoarseness was noted in two of our patients as the growth apparently involved the recurrent laryngeal nerve due to direct extension of the growth or to metastasis. Dysphagia was noted in one patient as the growth extended to and invaded the esophagus. This extension of the growth ultimately caused complete obstruction of the esophageal lumen. Weight loss is a late development and one which is seen in practically all patients. Apnea and suffocation will eventually develop if the growth cannot be controlled.

Report of Case

Mrs. L. L., our most recent case, is a white female, age 60, who was sent to us Sept. 13, 1946, by Dr. Kellie Joseph, of this city, for bronchoscopic

examination. Her chief complaint was "asthma," from which she had suffered eight years.

At the onset of her illness, she had consulted an internist who had fluoroscoped her thorax and declared the chest to be normal in appearance. In 1944

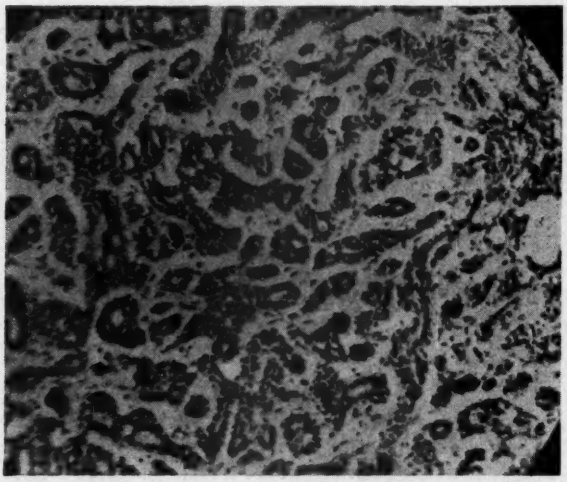

Fig. 1

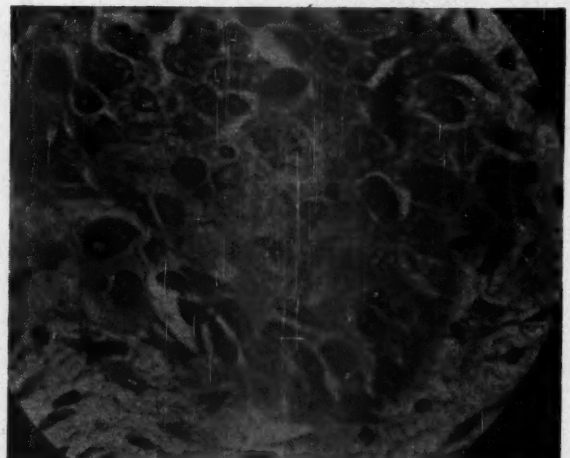

Fig. 2

she had hemoptysis of about a dram of blood, after which she noted blood streaked sputum occasionally, with only one other moderately severe hemoptysis in January, 1946.

In December, 1945, she had had an attack of lobar pneumonia. In April,

1946, she had been hospitalized 7 weeks with what was diagnosed as virus pneumonia. An x-ray, just prior to her visit with us, revealed partial atelectasis of the left lung.

When seen in consultation with the writer, her chief complaints were shortness of breath and extreme fatigue on the slightest exertion. She had lost 8 pounds in weight in the past few months.

The family history revealed that her grandfather died of tuberculosis and an uncle had severe asthma. The past history revealed that the patient had radium treatment in 1934 for "tumor on the neck of the womb."

Physical examination showed a well nourished and well developed elderly

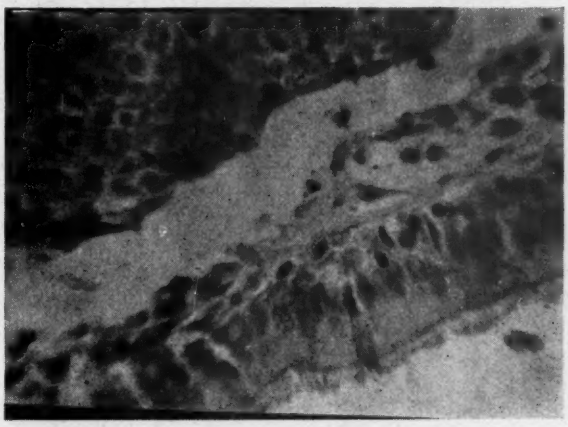

Fig. 3

female, weighing 118 pounds. Height 62½ inches. Temperature 100.6. Pulse 100. Respiration 20. Blood pressure 180/90. The significant findings were limited to the thorax. The heart sounds were normal, but the right border of the heart was found at the left sternal border, and the point of maximum cardiac impulse was in the left anterior axillary line at the fifth interspace—showing considerable cardiac displacement. The right lung was clear. The left lung presented greatly diminished breath sounds over the lung field anteriorly and a few posttussic rales in the extreme apex posteriorly. There was no wheezing.

The laboratory examination: Hemoglobin 80 per cent (Dare), sedimentation rate 30 mm. (Cutler), urine normal, blood Kahn negative, five sputum examinations for tuberculosis negative. Sputum culture showed long chained streptococci and gram negative diplococci as dominating organisms.

The patient was bronchoscoped on September 11. Under local anesthetic a 7 mm. bronchoscope was passed. Larynx was normal. Just above the bifurcation of the trachea a large growth was encountered which arose from the left posterolateral wall of the trachea, and filled approximately 80 per cent of the tracheal lumen. It extended downward obstructing the left main bronchial orifice. A biopsy specimen was taken for microscopic examination.

Pathologic Report: "Several fragments of fairly firm tissue, irregular in

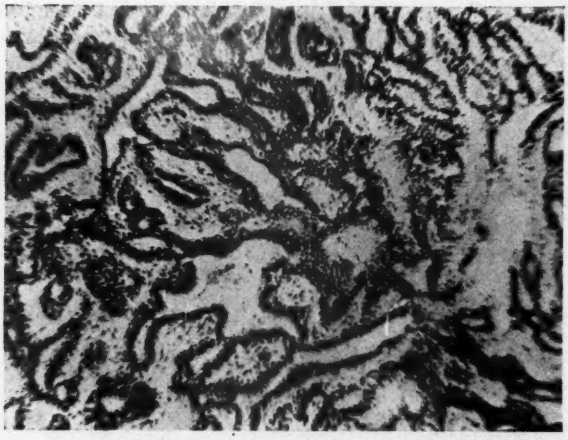

Fig. 4-a

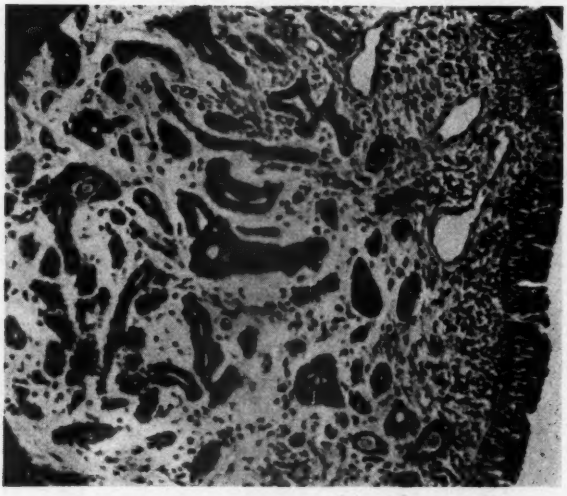

Fig. 4-b

shape and size, pale white, and having an appropriate volume of 1 c.c. (One Block). Microscopic Examination: The stroma has been invaded by masses of compactly arranged cells which are alveolar in character forming central lumina lined by cylindrical or cuboidal epithelium. These cells are ovoid in shape, having a light refractile cytoplasm and a darker, centrally placed nucleus within which mitosis is not seen. These alveolar arranged masses of cells are separated by very loose, myxomatous type of stroma within which small petechial hemorrhagic focal areas are present. The tumor grows in strands of epithelial cells with definite lumina of glands. The cells are quite uniform in size and do not show mitosis to any extent. Beneath these cords there is deli-

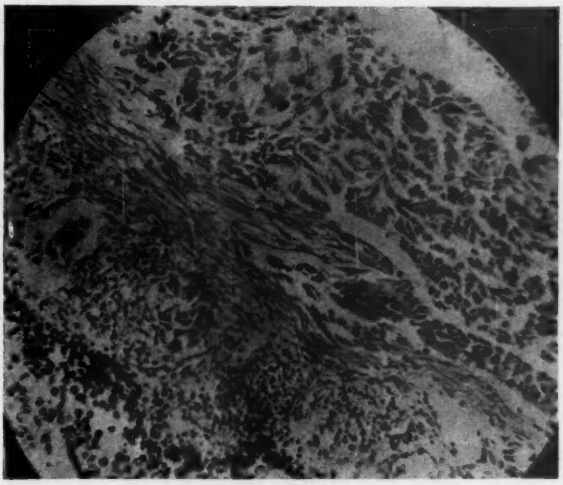

Fig. 5-a

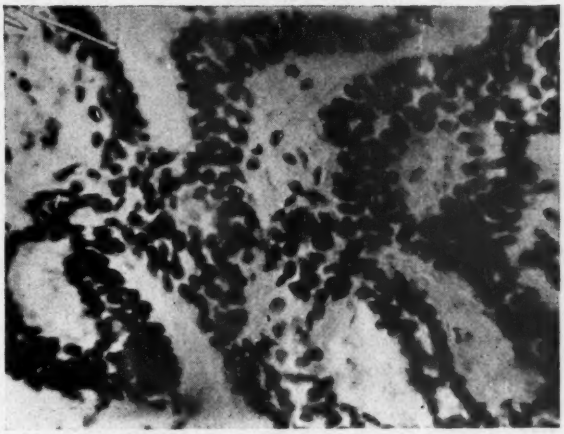

Fig. 5-b

cate connective tissue. The appearances are those of carcinoid of the trachea such as is described in Foot's PATHOLOGY AND SURGERY (J. B. Lippincott Company, 1945, Philadelphia, London, and Montreal). The appearances are rather like the carcinoid of the appendix or small intestine. We have not actually done a silver stain on this section so our diagnosis of carcinoid is only on morphologic similarities to a published case. It should be said further that the appearances are much like those of the so-called adenomas of the bronchus."

On September 17 the patient was bronchoscoped with an 8 mm. instrument and the tumor was partially removed with biting forceps and as thoroughly cauterized with electrocoagulation as deemed advisable at that time. Post-

operatively there was considerable improvement, and a definite partial re-expansion of the left lung.

Dean[8] states, "In the trachea as in other organs lined by pseudo-stratified columnar epithelium, there may occur a tumor microscopically indistinguishable from basal cell carcinoma of the skin. Great confusion has arisen concerning this tumor because of the multitude of names it has been given, depending on certain minor variations in architecture. Cylindroma, adenoid cystic epithelioma and adenocystic carcinoma are other names for the same tumor. These tumors often arise from the posterior tracheal wall just below the glottis. Their slowness of growth is evidenced by the fact that all cases reported had cough, stridor or dyspnea for one year or longer before the true nature of the lesion was discovered. A large percentage record treatment for asthma for varying lengths of time."

Diagnosis and Treatment

Diagnosis is most easily made upon bronchoscopic examination, visualization of the growth, biopsy and microscopic examination of the tissue removed. Our experience leads us to believe that any patient with cough, dyspnea and blood streaking of the sputum should be bronchoscoped immediately. The most satisfactory means of treatment is fulguration of the growth by means of electro-coagulation through the bronchoscope, accompanied by the aid of deep roentgen ray therapy.

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CARCINOMA OF THE PROSTATE GLAND

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CARCINOMA of the prostate is a disease which should be of considerable interest to the general profession because (1) it is very common among men of cancer age, (2) diagnosis can usually be made without complicated procedures and studies, and (3) much can be done to make the patients more comfortable, to minimize complications, and to lengthen life.

The importance of this malignancy is well illustrated by its very high incidence. Young has stated that one-fifth of all the male patients who seek relief from obstruction at the vesical neck have carcinoma of the prostate. Rich[1] in 292 autopsies on men over 50 years of age, found carcinoma of the prostate in 41 cases, or 14 per cent. This figure is striking but becomes even more so when it is realized that over two thirds of these cases were not diagnosed antemortem, because the tumor was too small to produce symptoms or to be palpable on rectal examination of the prostate. Moore,[2] in a clinical study, found carcinoma in approximately one fifth of 252 subjects between the ages of 41 and 90. As the average life span increases more patients attain the cancer age. The age of the average prostatic cancer patient ranges between 65 and 70 years. The expert urologic consensus is that approximately 14 per cent of all males past 44 years have carcinoma of the prostate. In less than one half of cases, there is no appreciable benign hypertrophy, either glandular, stromal or muscular, associated with the cancer, but in most cases there is such an association. Therefore, the possibility of carcinoma must be kept in mind in every patient with prostatic hypertrophy. Although carcinoma may begin in any prostatic lobe, about 75 per cent have been shown to begin primarily in the posterior lobe. This is the portion of the gland which ordinarily does not participate in benign adenomatous hypertrophy. The posterior lobe of course is the one most easily palpated on rectal examination, thus allowing early palpatory evidence of the malignancy, even though it be of very small size.

By the time most carcinomas of the prostate attract the patient's attention by producing urinary symptoms, the malignancy has often progressed to the point where curative therapy is out of the question. The diagnosis of early curable cases therefore is primarily the responsibility of the family physician. A carefully performed rectal examination should be carried out on every male patient over

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the age of 50, regardless of the presence or absence of urinary or rectal symptoms. The size of the prostate, and even more important, any induration of the prostate, should be carefully noted. Prostatic carcinoma is recognized by its hardness—any indurated area approaching the typical stony hardness should be suspected and thoroughly investigated, even though it be small in size. The small localized malignancy which has not progressed beyond the prostatic capsule offers the best chance for cure by radical perineal prostatectomy. But even in the less ideal cases where the malignancy has spread out beyond the confines of the capsule and surgical cure is no longer possible, there is a good deal that can be done, at least temporarily, to arrest the progress of the disease, thus prolonging life and adding comfort to the patient's remaining months or years.

Carcinoma of the prostate has a marked predilection for metastasizing to the skeletal system. In some cases the presenting symptom is one referable to this system and too frequently the unfortunate diagnosis of "arthritis" is made without further investigation. The bony metastases are readily demonstrated by plain roentgenograms—the bones of the pelvic girdle and the lower lumbar spine are most frequently involved. Pathologic fracture can occur and a number of cases have been reported in which there were no signs or symptoms of the malignancy other than the fracture.

There is a rather widespread erroneous impression that hematuria is a sine qua non in the diagnosis of carcinoma of the prostate. This is far from the truth, as numerous investigators have reported series in which hematuria was a comparatively insignificant manifestation of the disease. Indeed, some cases have no urinary symptoms at all and the disease is discovered by routine rectal examination performed in the course of a general investigation. The usual urinary symptoms, when present, are frequency, nocturia and difficulty of urination. In the more advanced cases pain due to osseous metastases may be the predominant symptom, with loss of weight, constipation, anemia, etc.

A recent and very valuable adjunct in the diagnosis of prostatic carcinoma is the elevation of the serum acid phosphatase. In 1935 Kutscher and Wolbergs[3] detected the presence of an enzyme, phosphatase, in the prostate. In the following year Gutman, Sproul and Gutman[4] found the same substance in bones containing metastatic prostatic cancer. These workers further established the fact that the blood contained both alkaline and acid phosphatase. Gomori[5] studied the distribution of acid phosphatase in normal and diseased tissues and showed that the normal adult prostate contained only

the acid phosphatase. He also stated that the malignant prostate contains more acid phosphatase than the normal gland. Apparently, the level of the serum acid phosphatase is not increased as long as the cancer remains within the prostatic capsule. However, as soon as the cancer cells grow beyond the confines of the prostate they increase the amount of enzyme in the circulation. This increased level of serum acid phosphatase is of specific diagnostic value as no other cancer produces such an elevation. Paget's disease of bone sometimes produces an elevation of the serum acid phosphatase but the alkaline phosphatase is also greatly elevated. This is not so in carcinoma of the prostate. Phosphatase is measured in terms of Bodansky or King-Armstrong units.

The modern treatment of prostatic cancer resolves itself into three categories—(1) curative surgical (2) palliative surgical and (3) endocrinologic.

Radical perineal prostatectomy offers the only known hope for cure in cancer of the prostate. Young,[6] and also Colston,[7] reported that in about one half of the cases subjected to radical perineal prostatectomy there were no recurrences after 5 years and that many cases had been followed over 10 or more years without any evidence of recurrence. Unfortunately, few cases are likely candidates for radical operation because, as stated above, the cancer has usually escaped the confines of the capsule by the time the diagnosis is made. However, there is some evidence which indicates that perhaps some of the cases which were thought to be too far advanced for radical operation might be made operable by preoperative hormonal therapy, either castration or estrogen administration. Vallett,[8] described a case in which the prostate was the seat of an extensive malignant process. Orchiectomy was done, with marked diminution in the extent of the tumor mass. Radical perineal prostatectomy was subsequently performed. Colston[9] has reported 4 cases in which the whole prostate was involved in the malignant process, but there was no evidence of metastases. The administration of diethylstilbestrol resulted in a marked regression of the prostatic tumor mass. Radical operation was carried out without any particular difficulty. Colston believes that "with selected endocrine therapy more and more cases will be suitable for complete radical extirpation."

In the second category, the palliative surgical group, belong those cases in which the cancer is obviously incurable but the obstructive urinary symptoms necessitate either removal of the offending portion of the growth by transurethral resection or diversion of the urinary stream by suprapubic cystostomy. These of course are

purely palliative measures and offer the patient only temporary relief of obstruction but no actual retardation of the malignant process.

It is the third category which at the present time holds the greatest interest for us. The discovery and practical application of an endocrinologic approach to the problem of prostatic malignancy is probably one of the most significant modern advances in the treatment of malignant disease. Over a century ago it was noted that the prostate underwent atrophic changes following orchiectomy. Fifty years later, White,[10] demonstrated the histologic changes in the prostate after castration in experimental animals and reported considerable clinical improvement after orchiectomy in a number of men with benign prostatic disease. Cabot[11] reported similar results 3 years later. Castration, however, did not prove popular and was soon discarded. It was not until a number of years later that a relationship between the sex hormones and prostatic malignancy was demonstrated. In 1935 Strohm[12] reported that the female sex hormones had a pronounced favorable effect on the symptoms of patients with carcinoma of the prostate. Counseller,[13] in the next year, reported diminution of pain in prostatic cancer patients after "sterilization" of the testicles by roentgen rays.

Perhaps the most outstanding contribution in this connection is that of Huggins.[14] After considerable laboratory animal experimentation, he performed orchiectomy on 21 patients with far advanced or metastatic carcinoma of the prostate. Of these, 4 patients died within 8 months and 2 were followed for only brief periods; the remaining 15 showed appreciable clinical improvement as evidenced by marked diminution of pain, increase in body weight, appetite, red blood cell and hemoglobin values, shrinkage of the primary lesion on rectal and cystoscopic examination, stabilization or regression of bony metastases in the roentgenograms, and decrease in the level of the serum acid phosphatase. (A five year followup on this group has recently been reported by Huggins.[15] Five of the original 21 patients are still alive. In four there is no clinical or laboratory evidence of cancer at the present time and one, the fifth case, is alive with slowly advancing prostatic carcinoma. This type of study of "closed series" is invaluable, as pointed out by Vest and Frazier[16] who recently reported their "closed series" of 74 cases and assembled comparative data on the series of 5 other groups of investigators.) There have been many other similar encouraging reports in the literature. In 1941 Munger[17] presented his work on "x-ray castration." He reported favorable results and pointed out that with this method the patient does not undergo the psychic disturbances that so frequently follow surgical castration.

Another substitute for actual surgical castration is the neutralization of testicular androgens by the administration of estrogenic substances such as stilbestrol and diethylstilbestrol. This form of therapy appears to have a very definite place in the treatment of prostatic carcinoma, particularly in those patients who refuse surgical castration or who are considered too poor operative risks. There is considerable difference of opinion as to the dosage and advocated dosages range from 1 mg. daily. Perhaps the most satisfactory results have been attained by administering the drug according to the patients' tolerance. Gastric irritation and transient swelling and tenderness of the breasts indicate too high dosage. Our practice is to administer intramuscularly 5 mg. of diethylstilbestrol daily for the first 2 weeks, then give 1 to 3 mg. stilbestrol per day by mouth as a maintenance dose. This has been found most satisfactory but is modified as necessary in individual cases.

There has been much written concerning the relative merits of castration and estrogenic therapy. Both procedures approach the same goal—namely, rendering the circulating androgens impotent. In the one case, the testicular source of androgen is removed; in the other case, the androgen is "neutralized" by the administration of estrogen. Surgical castration is usually more dramatic and pronounced in its effects. Pain, nausea and vomiting, and in a lesser number of cases, urinary dysfunction, may practically disappear within a very few days. The elevated serum acid phosphatase drops to normal, the patients feel and look better and there is a notable reduction in the induration, and frequently in the size, of the local prostatic cancer mass. Appetite improves—indeed, it has been reported that two thirds of these patients regain their lost weight. Approximately one fifth of patients obtain no relief from castration or estrogenic therapy.

Both castration and estrogenic therapy are accompanied by disagreeable features. Many of the younger patients complain of loss of sexual power and of reduction in size of the penis. A fairly frequent complication after estrogenic therapy is gynecomastia and erect tender nipples. This does not occur after surgical castration. In a few patients, the administration of stilbestrol by mouth produces nausea and vomiting. Edema is a rather rare complication, but in one of our recent cases the leg and ankle edema became so severe that the patient could not wear his shoes and became practically bedridden. Termination of the stilbestrol therapy resulted in a rapid disappearance of the edema. Deming[18] tells of 3 patients who developed acute diabetes mellitus, but he feels that this might have been due to metastatic lesions in the pancreas rather than to the estrogenic therapy.

Perhaps the wave of enthusiasm and optimism which followed the introduction of these endocrinologic methods of therapy was unjustified and unwarranted. There is no doubt but that these methods have added much to the welfare and comfort of prostatic cancer patients but the fact remains that no cures are obtained and all the benefits are temporary. As a matter of fact, there are some who question that the lives of these individuals are prolonged at all.

The role of the adrenals is not fully understood. Huggins and Scott[19] subjected four patients with prostatic cancer to bilateral adrenalectomy. All of these patients had had orchiectomy with temporary improvement. The first two patients died in shock 36 and 54 hours after complete adrenalectomy. The third patient died 11 days postoperatively. The fourth patient lived 116 days. There was a marked decrease in the urinary excretion of 17-ketosteroids after complete adrenalectomy. This work indicates quite definitely that the extragonadal androgenic depot in man is the adrenal. The authors conclude that this method is not practical in the treatment of prostatic cancer by antiandrogenic methods.

There is much investigative work which must be done, with careful followup studies, before a final verdict can be reached. Still, much has been gained, and many fundamental concepts are being formulated promising the eventual control of this very common disease in the not too distant future.

Summary

The general subject of carcinoma of the prostate is reviewed. Emphasis is laid upon the importance of adequate rectal examination in men over 50 years of age. Radical perineal prostatectomy is the only hope for complete cure at the present time. Newer methods of treatment are discussed with special attention to hormonal therapy—i.e., surgical castration and estrogen administration. The therapeutic effects of these methods are outlined.

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RECENT ADVANCES IN OPHTHALMIC SURGERY

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1. CORNEAL TRANSPLANTATION

The experience gained by successes and failures of corneal transplantation, and the evolution of newer instruments and improved technic have increased the effectiveness of this procedure in carefully selected cases.

Corneae from eyes of still-born babies are not a superior source, for recent studies have shown that such grafts are more likely to lose their transparency. Injured eyes, eyes with tumors involving the posterior segment only, and eyes from recently deceased persons provide satisfactory donor material. The best method yet found to preserve an eye is to immerse it in physiologic saline at a temperature of 3 to 4° C., but two days is the maximum it may be kept before using.

Before surgery is considered, careful examination must reveal that all other ocular structures are sound. The corneal opacity must be central and not too extensive. The clearer the area surrounding the corneal opacity, the more favorable the prognosis. There must not be the slightest inflammation of any structure of the eye. There must be no anterior sychniae. Corneal transplants are most likely to help in the following conditions: keratoconus, scarred cornea of interstitial keratitis and of gonorrheal keratitis, blood-staining of the cornea and some types of corneal dystrophies. When a dense leucoma extends over the entire cornea with vascularization, or if glaucoma is present, a corneal transplant is contraindicated.

Castroviejo's[1] double-bladed knife for cutting a square graft (fig. 1) has been used with much success. Corneal trephines are advocated by other ophthalmic surgeons, and Paton[2] has recently presented a trephine with several refinements. Recently, Guyton has devised a trephine powered by a dental motor. Green's automatic trephine is the writer's preference because the rapid cutting of the graft results in a more regular and smoother cut.

The donor graft is first cut from the eye and placed in a small shallow dish of normal saline. The section to be removed from the recipient's eye is then marked with an incision into Bowman's membrane, and the suture is placed around its margin. Castroviejo[1] has devised a special method in which the sutures are placed around this square graft. Paton uses two figure of eight sutures

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of different colors (fig. 2). Katzin[3] has devised a clover leaf design with one suture which holds the cornea with equal tension in all portions.

The anterior chamber is used as a safety space between the cutting edge and the lens. When the corneal section is completed,

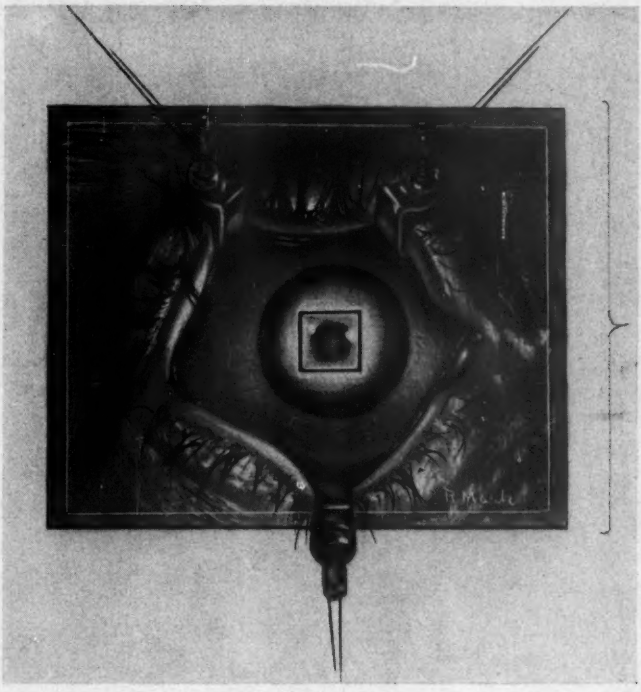

Fig. 1. Square section of corneal opacity to be removed, as devised by Castroviejo.

the aqueous flows out. The anterior chamber is immediately lost and the iris and lens come in contact with the posterior surface of the cornea. Any fibrous strands which remain attached to the cornea are divided.

The graft is set in place. The convexity of the cornea is usually apparent, but care must be taken that the epithelium faces anteriorly, the endothelium posteriorly. Paton has recently presented a fenestrated spatula which is excellent for this measure. The suture is then pulled in place and tied firmly. The aqueous usually

refills the anterior chamber rapidly, and the usual reaction is not severe.

The sutures are removed from five to eight days after the opera-

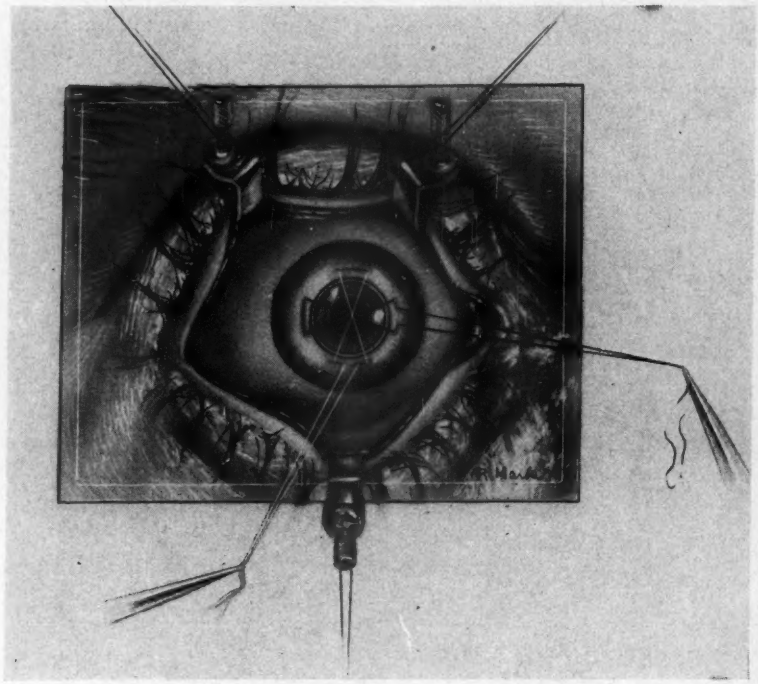

Fig. 2. Paton's double figure of eight sutures.

tion. If haziness of the cornea and loss of transparency occurs it is more likely to do so during the first month or two. Iliff has recently described the successful use of beta radiation to prevent postoperative granulation, and to inhibit the overgrowth of connective tissue. If the graft remains transparent for six months, it is likely to continue to do so. In the past ten years an improvement of vision has resulted in about 80 per cent of carefully selected cases.

2. Contact Lens for Unilateral Aphakia

Young patients with a traumatic cataract in one eye and elderly patients with a senile cataract in only one eye have often been advised not to have the cataract removed. This was because of the double vision which usually resulted when a spectacle lens was fitted over the operated eye. The double vision is due to two factors:

(1) The retinal image in the aphakic eye is larger by a third than the image in the fellow eye, and (2) more important, the pris-

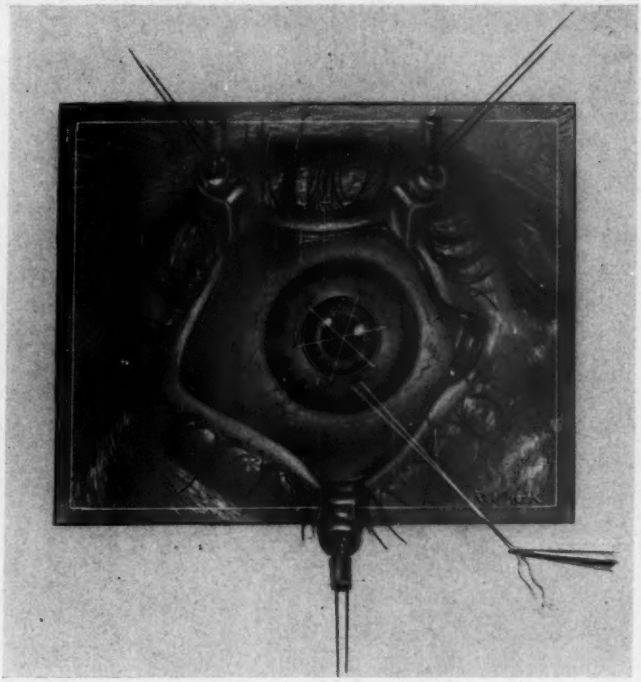

Fig. 3. Katzin's clover leaf suture.

matic error caused by the lens increases with the degree that the eye is turned from the primary position.

However, if a contact lens with the correct power is fitted to the operated eye, the sizes of the retinal images will be nearly equal. Since the contact lens moves about with the eye, no prismatic error occurs. The ocular criteria for attempting to re-establish single binocular vision by this method are corrected visual acuity of 20/30 or better and normal muscle balance.

The patient's intelligence has much to do with whether contact lenses are prescribed. They must be inserted beneath the lids with great care, for despite the relative softness of modern plastic materials, it is easy to abrade the corneal epithelium. It requires some practice to keep the buffer solution from escaping at the time of insertion. The patient's eagerness for such lenses must be evaluated for there are many difficulties to overcome in their fitting.

After this has been completed, several months may elapse before patients can develop enough tolerance to wear them continuously for six or eight hours. Despite the use of various buffer solutions, some eyes are unable to wear contact lenses for more than an hour. However, an aphakic eye frequently acquires the necessary tolerance more rapidly than keratoconus or myopic eyes do. Unless the type of work which the patient performs requires single binocular vision the time, effort and expense may not be justified. The writer examined one hundred soldiers with uniocular aphakia, and found only twelve he thought would benefit from contact lenses. These were prescribed, but a year later a few of these were found to be unsuccessful.

3. Scleral Resection

In the 17 years which have elapsed since Gonin showed how to cure retinal separation systematically, many improvements in the diagnostic study and refinements in surgical technic have been devised. There are several methods of applying diathermy electric current in the region of the tear. LaCarriere's and Kronfield's needles are used to make small diathermy punctures of the sclera in the region of the tear. Isolated "micropins" of Walker's or Pischel's have the advantage of maintaining normal tension until the procedure is completed. With this method the retina is less likely to be traumatized because it is displaced from the sclera by the interretinal or subretinal fluid. Weve's electrode and Rychner's modification of it are also in common use for surface coagulation.

The use of these and other methods for the usual idiopathic and traumatic separation has given satisfactory results of 75 per cent and upwards, as reported by many ophthalmologists. But there are yet other and more difficult types of retinal separation. Retinal separation in aphakia has an associated poor prognosis, and Linder's undermining operation of making several trephine openings in the region of the tear seems particularly indicated for this. There are other types of difficult cases in which the separated retina has become too small to fit the interior of the eye. This may be due to agglutination of a retinal fold or folds, or to shrinkage of the retina consequent to diffuse retinitis proliferans which in turn may have been caused by vitreous hemorrhage at the time of the retinal tear or following some operative procedure. In such cases the retina is shrunken. This makes the situation radically different from the ordinary retinal detachment, and necessitates a different surgical approach based on a different concept. Since the retina will not return to its proper place by the usual operations, the method of attack may more properly be the shortening of the

scleral shell to fit the smaller retina. For these cases the eyeball shortening operation is the only one that offers any hope.

Linder in 1933 reported this operation, a modification of the

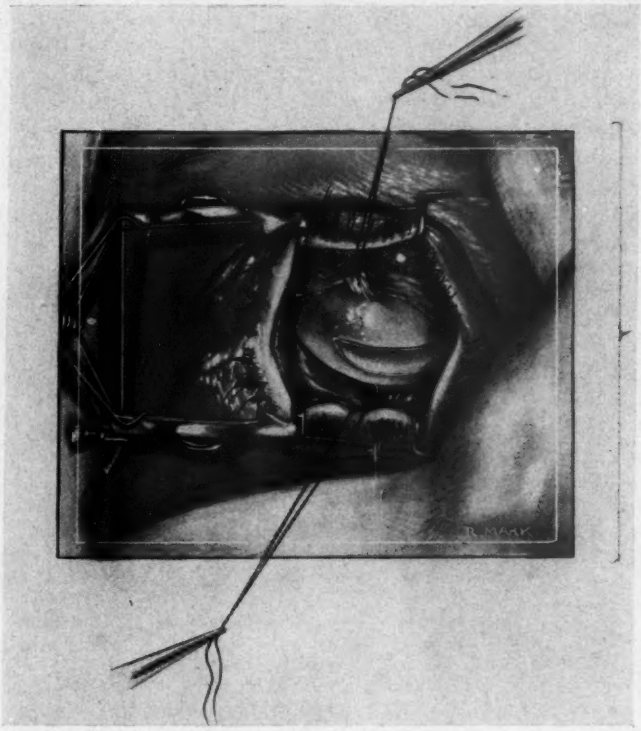

Fig. 4. Scleral resection. The suture in the upper portion of the drawing has been placed through the stump of the superior rectus tendon, and the suture in the lower portion of the drawing is attached to the inferior rectus muscle. An incision half way through the sclera has been made, showing the amount to be resected.

procedure originally suggested by L. Muller in 1903 for treatment of high myopia. He cited several cures and a number of improvements in apparently hopeless cases. The eyeball is shortened by an excision of a crescent shaped piece of sclera and rejoining of the cut scleral edges with sutures. The crescent is usually removed from the area of the greatest separation, which may be the upper or lower half of the globe, or nasally or temporally. It is cut from 2 to 6 mm. wide, concentric with and at a distance of 9 to 12 mm. posterior to the limbus. In length it may be from less than half to just more than half the circumference of the globe.

The sclera is laid bare and the rectus muscle over the area of largest detachment is temporarily divided.[5,6] With specially equipped dividers, the lines are marked off in the sclera. The sclera is cut halfway through its thickness. Mattress sutures are then placed 2 mm. apart through the anterior and posterior incisions leaving the flap free. After all of the sutures are in place the crescent of sclera is carefully cut out, pulling the sclera together as soon as a portion of it has been removed (fig. 4). When this is completed the rectus muscle is then rejoined and the conjunctiva is closed. Considerable conjunctival edema results but this regresses after six or seven days. The patient is kept in complete bed rest for at least two weeks and then stenopeic glasses may be substituted for the binocular eye dressings.

This procedure has also been successfully performed in cases of high myopia, and anterior and posterior scleral staphylomas. In certain instances it has returned vision which otherwise would have been lost.

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THE PROBLEM FOR THE ANESTHESIOLOGIST IN DEALING WITH THE MALNOURISHED PATIENT

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THE problems which arise for the anesthesiologist when surgical interference is unavoidable in the presence of malnutrition are dependent on the damage that various systems or parenchymatous organs of the body have suffered. Malnutrition is primarily the result of the lack of adequate nutritive material or nutralites available to the individual cell, some disturbance in metabolism preventing proper utilization of food, or an increase in the demand of the cell. Nutritive material or nutralites may not reach the cell because of inadequate intake or disturbance in absorption from the gastrointestinal tract. Malnutrition in patients seen at the Jefferson Hospital as a result of dietary deficiencies occurs most commonly in the poverty stricken group. Food fads and reducing diets, which are not properly supervised, have in recent years played a part. The ill effects of chronic alcoholism may be, and probably are, largely dietary.[1] Little evidence has been adduced to show that the ingestion of alcohol in the presence of adequate diet is injurious. The typical history of the malnourished alcoholic reveals the substitution of alcohol for food. Malnutrition appears secondarily in certain diseases. Anorexia in the chronically and critically ill may result in malnutrition. Lack of appetite, disturbance in passage of intestinal contents and lessened absorption may occur in disease of the gastrointestinal tract. Certain diseased states cause wasting in spite of diet adequate for normal individuals. Usually a high caloric diet will improve the nutrition in the presence of such conditions; i.e., tuberculosis and thyrotoxicosis where the metabolic demands are increased.

A low caloric diet will produce malnutrition, but the most serious damage to the body occurs when the protein intake is reduced, especially if such protein as is ingested is lacking in some of the essential amino acids, and if the diet is deficient in certain of the vitamins.[2] As a result of these deficiencies, or as a result of a combination of the deficiency plus an intrinsic defect, several definite disease syndromes may appear.[3]

Pellagra

Pellagra[4] is a disease attacking the skin, gastrointestinal tract,

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and central nervous system. The skin lesions are usually bilateral, characterized by roughened erythematous areas on the dorsum of the hands, knees, ankles, neck, axilla and perineal region. The roughened areas progress to desquamation and cracking of the skin; there is frequently pigmentation of these areas. The gastrointestinal symptoms begin as anorexia, burning of tongue, and abdominal pain, and lead to glossitis, stomatitis and gastroenteritis with ulcerating lesions. A fiery red, beefy tongue is diagnostic of pellagra in the absence of skin lesions. The central nervous system changes are largely of a psychoneurotic character. An anemia of severe grade, macrocytic in type, is frequently found. If pellagra is a disease resulting entirely from inadequate diet, it is the result of multiple deficiencies. Low protein intake or the intake of inadequate proteins plus insufficient vitamins, especially of the B complex, are found in the history of most pellagrins.

Gillman and Gillman,[5,6] of South Africa, have carried out an impressive series of liver biopsies on pellagrins which show that there is fatty change in early pellagra, leading in untreated cases to hemachromatosis and cirrhosis. In those patients, usually infants, who had a severe degree of fatty degeneration of the liver cells, they not only were unable to obtain cures with pellagra-preventing diet and the use of large doses of nicotinic acid, thiamine and riboflavin, but had a high mortality. It was necessary to add liver extract and/or desiccated stomach to effect cures. It is possible that these patients may have had celiac disease as a complication of pellagra.

György[7,8] showed in his experimental work with rats that liver damage, fatty changes and cirrhosis may be artificially produced by feeding them on diets deficient in proteins, especially when there was lack of methionine. Even on a deficient diet the addition of methionine and choline improved or returned the liver to normal. The addition of the amino acid cystine alone increased the damage, but cystine plus choline and/or methionine caused rapid regeneration of the damaged cells. A problem for research has been suggested along this line. We hope to have facilities to check the function of the liver—treat the patient with choline and methionine and check the liver function again before and after the administration of an inhalation anesthetic. The liver function tests in use today may not demonstrate damage unless there is more than 50 per cent of the liver not functioning. If we may assume that liver damage is uniform throughout the organ, then the use of aspiration biopsy would give us a more accurate picture. Iverson and Roholm[9] have described a safe and simple method for obtaining such specimens. If possible, we hope to obtain such biopsy specimens and check the

effects of amino acids and choline and the effects of various anesthetic agents.

A cure or remission in uncomplicated pellagra is seen following the use of a high caloric diet, especially of adequate protein and carbohydrates plus massive doses of nicotinic acid (one of the vitamin B complex).[4] Nicotinic acid (or the amide) is given in doses that vary from 50 to 500 mg. per day.

Beriberi[4]

Beriberi is a disease found most commonly in Oriental countries, characterized by a poor nutritive state, plus changes in the peripheral nerves. It occurs where the diet is made up exclusively of polished rice. The specific lack is low levels or absence of vitamin B_1 (thiamin). True beriberi is rarely seen in this country, but careful investigations of recent years have shown that polyneuritis of varying degrees is found more commonly than thought earlier and the neuritic signs will improve or disappear under intensive treatment with thiamine plus the usual high caloric diet.[10] In pellagrins, improvement on the previously suggested regimen may not be complete unless thiamine is added because of the multiplicity of the deficiency in the diet causing the characteristic picture. That is, there may be a polyneuritis in addition to the other symptoms. There are two types of beriberi: (1) the "dry" and (2) the "wet." The first is already described. In the "wet" type there is added an edema of dependent portions of the body and usually hypertrophy of the heart. Diagnosis[11] of beriberi heart disease is based on: (1) enlarged heart with normal rhythm, (2) dependent edema, (3) elevated venous pressure, (4) peripheral neuritis and frequently pellagra, (5) nonspecific changes in the electrocardiogram, (6) no other cause evident, (7) gross deficiency in diet of three or more months' duration and (8) improvement on a regimen designed to cure beriberi.

Ariboflavinosis

Ariboflavinosis, that is, the lack of the vitamin riboflavin, is characterized by loss of weight with weakness and lassitude. The external lesions are stomatitis, cheilosis and vascularization of the cornea. Pellagra preventing diet, plus nicotinic acid and thiamine may still leave a residue of these symptoms in pellagrins. Riboflavin is frequently necessary to effect a complete disappearance of the pathologic manifestations.[4,10] Ariboflavinosis is the most common deficiency found in this country.

Scurvy[12]

Scurvy results from a diet lacking or low in vitamin C. This dis-

ease is not common in this country, but low levels of vitamin C, due to diets restricted in the use of fresh fruits and vegetables—especially citrus fruits and tomatoes, are not uncommon. The symptoms of true scurvy are anorexia, lassitude, pain and swelling of the joints, usually the knees and ankles, the appearance of bruised areas, ecchymotic patches and frequently swollen, painful gums which bleed easily. These individuals have a pale greyish colored skin which is cadaveric in appearance. Anemias of varying degrees may complicate this disease, usually of a normocytic normochromic type. Correction in the diet with the addition of large amounts of orange and lemon juice or cevitamic acid will correct this symptom complex. It has been shown that where there are low levels of vitamin C, even without clinical signs of scurvy, tissue healing may be impaired.

Sprue and Macrocytic Anemia

Sprue is not clearly defined as a pure deficiency disease.[13] Malnutrition is part of the picture so that it must be included in this discussion although it is rare in this country. There is severe weight loss accompanied by diarrhea, characterized by foamy stools of foul odor and macrocytic anemia usually of severe degree. The general picture of this disease is said to result from altered absorption from the gastrointestinal tract. Macrocytic anemia[14] is due to a disturbance in the hematopoietic factors in the body, probably the lack of an essential substance stored in the liver. This essential substance is probably made up of the interaction of an intrinsic factor elaborated in the normal stomach and an extrinsic factor supplied by several foods: meat, eggs, wheat germ, rice polishings, liver, milk and yeast. The causes for macrocytic anemia are: (1) quantitative deficiency in intrinsic factor (pernicious anemia), (2) lack of extrinsic factor (pellagra), (3) lack of absorption from the gastrointestinal tract of the essential hematopoietic substance (sprue), (4) inability on the part of the liver to store the essential substance may occur in severe liver damage. Sprue can be improved by a diet aimed to treat general malnutrition, plus massive doses of vitamins and specific treatment for macrocytic anemia (this preferably should be a parenteral form of treatment because of the poor absorption).

Hyperthyroidism

The patients with thyrotoxicosis frequently present an appearance of malnutrition. They may be ingesting what appears to be an entirely normal diet, but because of the high metabolic rate it is not sufficient to maintain their weight. The problem for the anes-

thesiologist with these patients is very different from those with simple dietary deficiencies. They have an unstable nervous system, hypertension and cardiac involvement with accelerated pulse rate, cardiac dilatation and hypertrophy. Emotional excitement or fear may precipitate a "thyroid crisis." These patients tolerate large doses of preoperative sedative drugs, in fact, require them to allay fear and reduce the metabolic rate. Guedel has pointed out that in the induction of anesthesia, one must first overcome the metabolic resistance before anesthesia can be obtained.[15] These patients have an increased demand for oxygen and disturbance in carbohydrate metabolism. No operative procedures except the most urgent emergencies may be considered in these patients until their condition has been treated with the lowering of metabolic rate and pulse rate. Lahey recommends the use of thiouracil, 0.6 Gm. per day, until the metabolic rate is normal.[16] For 2 or 3 weeks before operative procedures on the thyroid, Lugol's solution is added to the medication. The last week the thiouracil is stopped. In less severe cases Lugol's solution alone is used or if there is a toxic reaction to thiouracil.

Infectious Diseases

Infectious disease may be the cause of malnutrition. There may be anorexia, or increased metabolic demand on the part of the cells, disturbed gastrointestinal function with vomiting and diarrhea and poor absorption from the tract. Pulmonary damage may be added to the problem of choosing the agent and method least likely to add to the burden of an already disturbed physiology.

Renal Damage

The question of renal damage in deficiency diseases has not been made clear. There is little mention of it in the literature. György finds that a hemorrhagic necrosis or cortical nephrosis follows the cirrhosis in his experimental low protein diets in rats.[7,8]

Resistance to Infection

"Lessened resistance to infection, leucopenia, depression of agglutinins and phagocytosis occurs in the presence of malnutrition." Experimental work seems to show that it is related to the general undernourishment rather than to the lack of a specific vitamin. There is some evidence to show that resistance is lowered by lack of vitamin A and raised by increased intake of this vitamin.[17]

Fluid Balance and Hypoproteinemia

Dehydration is frequently an accompaniment of malnutrition, particularly of the acute variety. There may be electrolyte imbal-

ance if there has been diarrhea or vomiting or if intestinal fistulæ are present. If the protein is sufficiently low to cause a hypoproteinemia, there will be abnormal amounts of fluid in the tissue. The knowledge concerning all of this complicated problem of malnutrition is constantly changing. Recent experiments indicate that, due to malnutrition per se, there is change in the wall of the capillary and that the edema of the tissues may not be caused by lowered plasma protein. They may be co-existing results of the same process.[18]

Lack of Minerals

Deficient diets will usually provide inadequate amounts of minerals. The most important of these are iron, calcium and phosphorus. The lack of iron may be sufficient to impose a hypochromic secondary anemia. This may be an addition to an already existing macrocytic anemia. The pellagra-preventing diet will supply adequate minerals providing the absorption from the gastrointestinal tract is normal. Parenteral administration may be necessary if there is not normal absorption. In children it may be necessary to add calcium and vitamin D to improve their condition.

The greatest number of patients showing poor nutrition do not have the classic symptoms of the deficiency diseases. Either the condition is acute enough that the signs have not appeared or although the diet is too low in calories to maintain weight, it supplies so near the amount of essential factors that the clinical symptoms have not appeared. The problem facing us is: Do these patients have the same damage to the systems and organs of greater or less degree? Would any individual, allowed only a pellagra producing diet over long enough time, develop the true clinical picture, or is there also a lack of an intrinsic factor due to something infectious, toxic or an inherent lack in the individual's economy that is brought to light by inadequate extrinsic factor?[28] Empirically we must conclude that damage, as described above, is present until proven otherwise.

The problem then of the anesthesiologist resolves itself into the proper handling of a patient who probably has anemia, liver damage, myocardial damage, unusual susceptibility to infection, the effects of hypoproteinemia, disturbances in blood pressure, frequently hypotension, occasionally hypertension, dehydration, electrolyte imbalance, and deficiency in minerals. His duty is to insure, in so far as possible, preoperative measures which will improve these abnormalities; to use methods and agents which will do the least to increase the damage to the already disturbed functions; and

to supply support throughout the operative procedure such that the postoperative period will not be unduly complicated.

Elective procedures are not to be considered unless they may contribute to the general improvement of the patient's condition and then only after the nutrition has been improved and specific treatment has been directed to the particular deficiency with clinical cure. If surgery is unavoidable, but not of such a nature as to call for immediate interference, an intensive period of treatment should be instituted with a view to supplying a high caloric diet and correcting the deficiencies in vitamins. Holman recommends preparing the patient, even in the normal nutritive state, for 1 or 2 weeks before entering the hospital, by means of a high protein, high carbohydrate diet of high caloric value.[19] In addition, he gives 6 haliver oil capsules per day and the juice of 4 oranges and 1 lemon supplemented by some form of the B complex vitamin. If there is jaundice and/or a low prothrombin level, he adds vitamin K and bile salts. On the day before operation he changes to parenteral injection of such vitamins as are available for parenteral use and continues this dosage in the postoperative period. The patient resumes the oral intake of vitamins as early as possible. If this is valuable in the individual who does not show evidence of malnutrition, how much more important when there is such evidence. In the presence of frank pellagra the patient should be put at bed rest, fed on a high caloric, high protein and carbohydrate diet plus massive doses of thiamine, nicotinic acid and riboflavin, crude liver extract and/or desiccated stomach. If there is macrocytic anemia, there is special indication for the use of liver and desiccated stomach. The use of folic acid routinely is not possible at present; it is available for experimental purposes only. Liver extract and dried stomach also have lipotropic action on the liver. To use the lipotropic amino acids, methionine and cystine, plus choline (a compound found in living tissue which lies somewhere between the vitamins and the amino acids and is sometimes included in the B complex) is beyond the facilities of most clinics at present.

The problem becomes increasingly difficult when there must be an immediate surgical procedure. What factors can be corrected in a short time? What can we do that will be of benefit to the patient? This paper was inspired by the comment of a research biochemist who said, "What anesthetic agent would you administer to a patient with pellagra who has acute appendicitis?" The anemia and therefore the lowered oxygen carrying power of the blood may be temporarily corrected by means of a blood transfusion. This will also serve to increase the plasma proteins. Glucose (5 or 10 per cent)

in distilled water may be used to correct the dehydration in the preoperative period and continued during the operation. If there is electrolyte imbalance, glucose in saline or Ringer's solution may be used. There are solutions containing amino acids, glucose and saline on the market which will also aid in correcting the protein deficiencies. Vitamin C, 100 mg., may be injected as it has been reported to aid in the healing of tissues, and vitamin K if there is jaundice. It is obvious that liver damage and myocardial damage cannot be corrected in any time less than weeks or months and these defects are important in our choice of anesthetic agent and method.

Premedication

Undernourished individuals other than the thyrotoxic patient will usually have a low metabolic rate. They will appear older than their chronologic age. Unless excessive fear and emotional excitement lead one to believe that the rate has been temporarily increased, the amount of sedative drug used for preoperative preparation should be smaller in amount than for the corresponding normal patient. We have made it a rule in the use of morphine, for example, to prescribe only 1/12 to 1/8 grains (0.005-0.008 Gm.) for patients 60 years and over, or for those who give the appearance of being this age, and only 1/16 to 1/12 grains (0.004 to 0.005 Gm.) for those over 70 years. An extremely undernourished patient of 40 may give all the signs of being a man of 60. No absolute rule can be given for the quantity of sedative drugs; each case must be individualized, but care should be used not to depress the undernourished individual too greatly. At the same time we must not lose sight of the possibility of increased metabolic rate and if there is fear and emotional excitement, the amount of premedication should be increased.

Local and Regional

Novocaine and allied compounds used for local infiltration or nerve block will cause the least disturbance to the liver, oxygen carrying power of the blood, and damaged myocardium if the patient is protected by moderate sedation from untoward reactions related to fear. Wherever practical, these should be the agents and methods of choice.

Intrathecal injection of novocaine or other agents suitable for spinal anesthesia will be contraindicated if there is hypo- or hypertension[20] or myocardial damage. In the presence of severe anemia the use of spinal anesthesia is also questionable because of the decrease in oxygenation that follows the vasodilatation with slowing of circulation and lessened ventilation. The advantage of spinal

anesthesia is the relaxation that follows and the absence of any ill effect on the liver. For procedures in the abdomen below the level innervated by the tenth thoracic nerves and on the lower extremities, it is the anesthesia of choice if the above conditions are not present or are minimal. The dosage of the drug should be reduced from the usual quantity used for a similar case and age. Fractional spinal anesthesia allows the use of very small amounts of procaine in repeated doses as needed. This method has obvious advantages over the use of a single dose.

Inhalation Agents

Of the inhalation agents we must choose only those which are potent enough to allow for a high percentage of oxygen and which will not add damage to an already deficient liver or myocardium. Nitrous oxide and ethylene are of such low potency that relaxation cannot be obtained without some degree of anoxia. Ether[21] as the sole agent is questionable because of its temporary interference with liver function and the lessened carbon dioxide combining power of the blood. If there is pulmonary congestion or damage, whether from heart insufficiency or from disease of the lungs, irritating agents should be avoided. It is an open question as to the use of ether in the presence of pulmonary tuberculosis. Some clinics prefer ether even in the presence of tuberculosis for intrathoracic surgery. We have usually avoided its use in pulmonary disease, but it cannot be said to be contraindicated in view of this acceptance of its use. Certainly the oxygen must be at an increased level to compensate for the decrease in oxygen absorption through the alveoli.

Chloroform[21] produces the same temporary liver dysfunction as ether and may cause central liver necrosis. Experimental work on dogs, which have been fed a deficient diet, shows that the liver is unusually sensitive to chloroform poisoning. Chloroform also acts directly on heart muscle so that there is decreased cardiac output and it sensitizes the heart to the irregularities induced by epinephrine.

Cyclopropane is very nearly the ideal inhalation agent; it is potent enough to allow of high percentage of oxygen; no liver damage can be demonstrated following its use. Cyclopropane has the disadvantage of causing cardiac arryhthmias in certain individuals or in certain concentrations. The pulse rate tends to become lower with cyclopropane.[22] It may become unduly slow, dropping lower than 56 per minute. Not infrequently irregularities develop. There may be extra systoles occurring with the decreased rate or the pulse may become very rapid (120 to 140 beats per minute) and paroxys-

mal tachycardia or an irregularity suggesting auricular fibrillation may develop. The conductive mechanism is altered, the normal pacemaker is inhibited and impulses arise from ectopic points along this mechanism. Reducing the concentration will frequently cause the rhythm to return to normal. The addition of a small amount of ether is said to stabilize the conductive mechanism of the heart beat. Cyclopropane, like chloroform, sensitizes the heart to the irregularities caused by epinephrine.[23]

Intravenous Anesthesia

Sodium pentothal[24] has been contraindicated in the past in the presence of liver damage and severe anemias. Further investigation leads us to believe that pentothal is not broken down by the liver and is not dependent on normal liver to prevent prolonged sleep nor does it add to liver damage unless anoxia is a complicating factor. It is recommended that inhalations of oxygen or nitrous oxide and oxygen 50/50 ratio be used with pentothal anesthesia at all times. If it is to be used in the presence of malnutrition with its accompanying anemia, this recommendation is doubly important. Its use should be restricted to procedures that do not require extremes of relaxation.

Probably the best approach is by the use of a combination of methods such as subarachnoid block of only a sufficient level to insure relaxation, supplemented by a light general anesthesia of cyclopropane and oxygen or sodium pentothal and oxygen to prevent intra-abdominal reflexes that require higher levels of paralysis. For operative procedures in the upper abdomen we may use abdominal field block or intercostal block, supplemented by cyclopropane anesthesia, or curare (60 to 100 mg.) used with cyclopropane. If local block is used with cyclopropane, the solution must not contain epinephrine. The level of inhalation in all of these combinations can be and should be maintained in lower first plane of the third stage or the upper levels of second plane; that is, at about the point that the eyeballs cease to oscillate. Maintenance of a patent airway is of extreme importance to insure that anoxic anoxia is not added to the anemic anoxia. An endotracheal tube may be indicated to insure the patency of the airway. If this is so, it will be necessary to have the level of anesthesia definitely in the second plane of the third stage to avoid laryngeal or bronchial reflexes or to use topical anesthesia on the pharynx and larynx before inserting the tube.

Summary

1. The causes of malnutrition have been summarized.

2. The clinical picture of some of the "deficiency" diseases has been presented.

3. The conditions of malnutrition which must influence the choice of anesthetic are: liver damage; anemia, hypochromic or macrocytic; myocardial damage; hypo- or hypertension; thyrotoxicosis; and renal damage.

4. Preoperative preparation of the patient to improve the damaged functions has been discussed.

5. The indications and contraindications of the more commonly used agents and methods have been discussed.

6. A suggestion for future experimentation has been made.

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FUNDAMENTALS IN SURGICAL PREPARATION OF THYROTOXIC PATIENTS

Use of Thiouracil

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THE hyperthyroid patient presents many unique features of management and the responsibility for preparation of this type for surgery should be that of both the internist and the surgeon. Each patient should have a complete general examination. This includes repeated metabolism tests, laryngoscopic examination, roentgenologic studies of the thorax to determine the presence or absence of substernal or intrathoracic goiter. Tests for hepatic and renal functions should be performed when visceral changes are suspected and an electrocardiogram should be resorted to as an aid in evaluating the extent of cardiac damage. Associated conditions such as diabetes, tuberculosis, nephritis, and pregnancy must be detected and given individual consideration.

The basic factors in the preoperative care include rest, high caloric diet, adequate intake of fluids, and the administration of iodine or thiouracil.

Physical and Mental Rest

The patient's activity and time spent in bed are gauged by the severity of the disease and by any associated condition. The average patient is up and about until the day of surgery, but he is advised to take afternoon naps and to avoid over-exertion. The patient in poor condition is confined to bed but as he gains strength he is encouraged to be up a part of each day.

Sedation is desirable to insure rest but its routine use is discouraged. The barbiturates in small doses, and occasionally the bromides, are utilized for this purpose. The patient and his friends are warned of the detrimental effect of undue noise or excitement. The thyrotoxic patient must enjoy both mental and physical rest, with avoidance of emotional or psychic stress, and with controlled physical activity.

Diet

The increased metabolic activity of the toxic goiter patient demands a greater number of calories for each cell of the body. As a result, the food requirements increase two to three-fold over nor-

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mal. The caloric intake of these patients should vary from 4000 to 6000 calories daily and the patient should be encouraged to consume food as long as he is capable of doing so. Occasionally the administration of a 5000 to 6000 caloric diet will not produce the desired weight gain and it becomes necessary to supplement oral feedings with the administration of intravenous glucose and amino acid solutions. The daily vitamin requirement of the patient should be met, especially thiamine chloride, and in severe deficiency states liver extract should be given intramuscularly. The nutritional balance of the patient must be established with full consideration directed toward the markedly increased metabolic rate. The dietary requirements are easily met in a patient whose excessive metabolic activity has been controlled with thiouracil.

Cardiac Complications

The patient with cardiac decompensation is given active treatment to relieve the congestive failure before an operation is performed. The administration of iodine or thiouracil and rest in bed will relieve the majority of cases. When this procedure is not sufficient, ammonium chloride, aminophyllin, and occasionally a mercurial diuretic, may be given to rid the patient of his edema. There are various opinions as to the advisability of using digitalis. Pemberton[1] has indicated the preference of omitting the use of digitalis in this class of patients except for those who fail to compensate without bed rest. Keeton[2] on the other hand feels that digitalis should be used in therapeutic doses when heart failure exists.

In addition to the above methods of combating congestive failure, sufficient food must be supplied to afford needed calories and to replenish depleted protein reserves. Adequate quantities of vitamins must be added, especially thiamine chloride. In patients with long standing hyperthyroidism one should consider the possibility of increasing the protein intake with amino acid supplements either orally or intravenously. The fluid intake, by mouth or parenterally if necessary, should be sufficient to prevent dehydration and to facilitate the dissipation of the body heat.

The determination of how effective treatment has been to overcome heart failure can be aided by several means. The physical examination should show a removal of the signs of edema in the lungs, abdomen and dependent extremities. The presence of swollen, thickened skin of the ankles and other parts of the body, rales in lungs or edema of the abdomen indicate the need for further treatment, including diuresis. There are several laboratory tests which can be of assistance in estimating the competency of the

right side of the heart. If the venous pressure is normal, or the arm-to-tongue circulation is not excessively prolonged, or if measurement of the vital capacity reveals a value of more than 70 per cent the surgeon may consider the patient adequately compensated. It is necessary that the results of these tests be interpreted in the light of other clinical evidence.

Auricular fibrillation is seen quite often in patients undergoing thyroidectomy and it only occasionally requires further treatment than rest and medication with iodine or thiouracil. In cases of chronic fibrillation the patients are usually comfortable and may be oblivious to their cardiac irregularity. Chronic fibrillation is usually associated with a sufficient degree of cardiac decompensation to elevate the venous pressure to a level high enough to facilitate the filling of the ventricles and consequently to maintain a satisfactory cardiac output. In contrast to this picture a bout of paroxysmal fibrillation may reduce the cardiac output due to the ineffectual auricular systole to fill properly the ventricles. The absence of an elevated venous pressure as associated with the cardiac decompensation in chronic fibrillation leaves the patient without a compensatory mechanism. If the bout of paroxysmal fibrillation is of moderate or severe character, quinidine should be promptly administered in doses sufficient to restore the normal cardiac rhythm.

In bouts of paroxysmal auricular flutter there is a similar danger of cardiac collapse due to the great reduction in the cardiac output. The drug of choice in treatment of auricular flutter is digitalis. Adequate doses of digitalis should be given to increase the auriculoventricular block and reduce the ventricular rate.

Diabetes

Diabetes mellitus and hyperthyroidism, either primary or secondary, are two separate and distinct disease entities, are fundamentally different in chemistry and are mutually antagonistic. Some of the beneficial effects of insulin are due to its inhibitory action on both glycogenolysis and gluconeogenesis. It follows that the action of insulin and thyroxin are antagonistic. Therefore insulin lack-diabetes mellitus and thyroxin excess-hyperthyroidism are basically different. Hyperthyroidism, with its elevated basal metabolism and increased glycogenolysis, imposes an added burden upon the inefficient carbohydrate metabolism of the diabetic patient. The combination of excess thyroxin and diminished insulin may activate a latent diabetic or project a mild diabetic into a severe diabetic. These two basically different diseases should not be allowed to exist or continue together over a long period of time in the same patient.

The fact that hyperthyroidism is so frequently linked with diabetes is under no circumstances a contraindication to modern thyroid surgery. Hyperthyroidism is the most immediate problem and should be corrected surgically as soon as the patient can be adequately prepared. Surgical therapy or surgical intervention should be for the purpose of carrying out a sufficient resection of thyroid tissue in order to produce a low normal or a slightly minus basal metabolic rate.

The occurrence of hyperthyroidism in the diabetic necessitates observation of the patient by both the internist and the surgeon. The preoperative treatment requires bed rest, rational diabetic diet, an adequate amount of insulin, the overcoming of dehydration by an adequate water intake by means of intravenous administration of normal saline, Ringer's solution or distilled water in 5 per cent dextrose solution, and the preoperative administration of iodine or thiouracil. The caloric requirements are 80 to 100 per cent higher than the patient's basal diet and diets of this order must be given the patient and the insulin increased as needed. It is not necessary to have the urine sugar-free but it is desirable to have the urine free of acetone and diacetic acid and the blood sugar should approach the high normal levels. The pre- and postoperative care of this type patient must be constant and detailed as the metabolic disturbance may be severe following surgery.

The Use of Iodine and Thiouracil

The administration of iodine or thiouracil is the most important factor in the preoperative preparation of hyperthyroid patients. The use of iodine as advocated by Plummer[8] for the preparation of these patients has saved many lives. Since the advent of thiouracil, however, iodine is being reserved for the mild and moderately severe states of hyperthyroidism and as an adjunct in final stages of preparation with thiouracil.

Ten minims of Lugol's solution are given 3 times daily in water, fruit juice or on dry toast. The therapy is usually continued over a period of 10 to 14 days, but if satisfactory clinical improvement has not been attained in this time, the medication should be continued over a longer period. The maximal improvement in the average case is obtained after 10 to 12 days of treatment; however, in certain cases this requirement does not reach its maximum for 2 to 3 weeks. In children the period of preparation is more than double that of the adult.

Thiouracil

The administration of thiouracil as introduced by Astwood,[4] and confirmed clinically by Lahey,[5] Clute,[6] Drennen,[7] and others, has permitted the surgeon to treat patients with a severe grade of toxicity with a greater range of safety. Thiouracil requires a longer period of treatment than that noted in iodine therapy but the decrease in toxicity is much more pronounced. Lahey[8] has advanced the rule of administering thiouracil for a period of one day for each degree of elevation of the basal metabolism rate above normal. For example, a patient with a basal metabolic rate of +55 will require approximately 55 days of thiouracil therapy to bring the basal metabolic rate to normal. Thiouracil is administered in the total daily dose of .6 Gm., .2 Gm. at 7 A.M., 3 P.M. and 10 P.M. Recently we have been treating patients with .4 Gm. total daily dose administered in equal amounts at 7 A.M. and 7 P.M. with satisfactory results. During the 3 weeks' period immediately before operation Lugol's solution is administered in an effort to reduce the friability of the thyroid gland found at surgery when the patient is treated on thiouracil alone. The week before surgery the thiouracil is discontinued and the patient is treated finally with iodine.

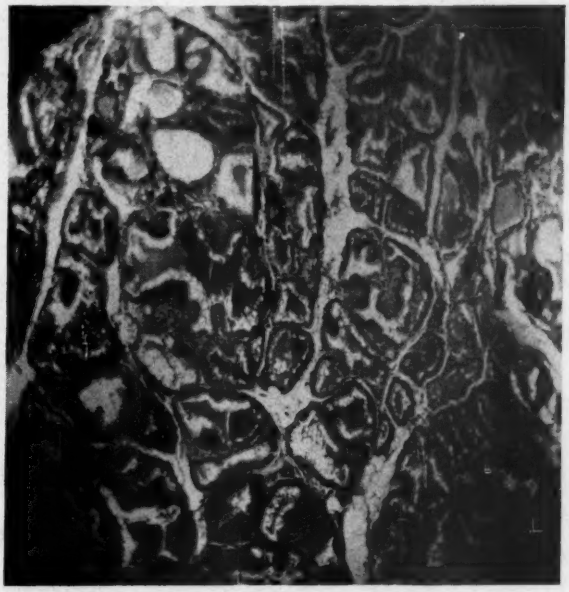

Fig. 1. Low-power view of the thyroid gland of a patient who received thiouracil treatment.

The danger of agranulocytosis or leukopenia developing while thiouracil is being administered is the greatest hazard of this form of therapy. Agranulocytosis has been reported as early as the

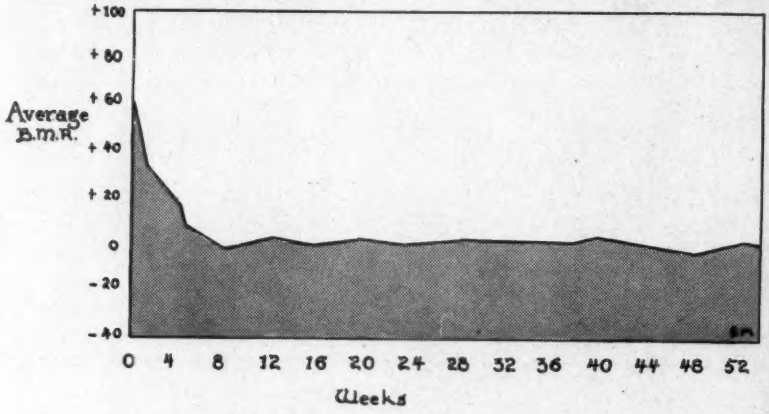

Fig. 2. Response of basal metabolic rate in 28 cases of moderate to severe thyrotoxicosis under thiouracil or thiobarbital medication.

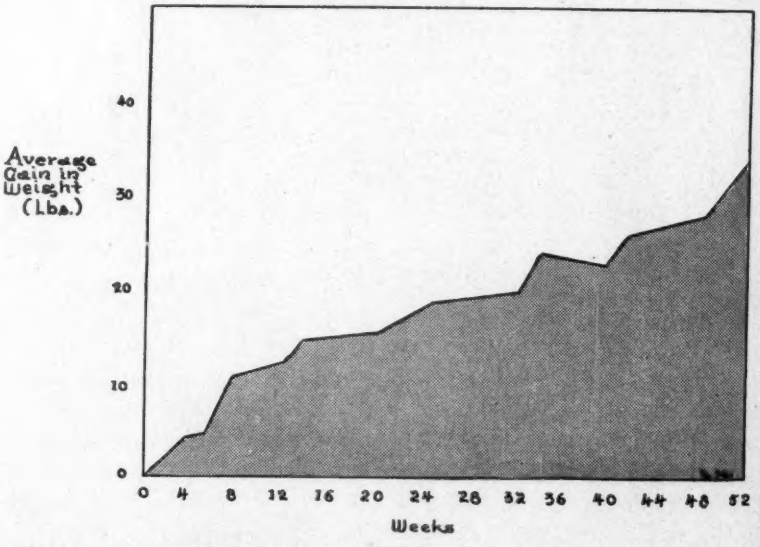

Fig. 3. Average weight gain in 28 cases of moderate to severe thyrotoxicosis under thiouracil or thiobarbital medication.

second week and as late as the ninth month and usually develops quite suddenly. Kracke[9] advises white cell and differential counts 2 or 3 times a week during the first month of treatment and weekly

thereafter in an effort to detect as early as possible changes in the blood picture. Other toxic manifestations which occur under the treatment of thiouracil include fever reactions, skin eruptions, scleroderma and swelling of the salivary glands. In patients who manifest minor reactions of sensitivity to the thiouracil it may be changed to thiobarbital with alleviation of the symptoms.

The histologic picture of the thyroid gland in patients who have been treated with thiouracil is one of hyperplasia. The individual cells are of the tall columnar type with mitosis very much in evidence and there is a marked papillary infolding of epithelial cells with a decided loss of colloid from the follicles as shown in Fig. 1. This picture is brought about by the inhibiting effect of thiouracil on the manufacture of this normal thyroid hormone. The resulting increase in activity of the thyroid-stimulating pituitary hormone brings about hyperplasia of the thyroid cells but does not produce an increase in the thyroid hormone, which is in fact reduced to subnormal levels.

Thiouracil reduces the elevated metabolic rate of hyperthyroidism to normal if it is administered over a sufficient length of time, and there is a gradual disappearance of all the hyperthyroid manifestations except those of the eyes when eye signs are pronounced before the treatment is begun. The rapid decline in the basal metabolic rate and the gradual increase in the weight of the patient are demonstrated, respectively, in Figs. 2 and 3. In addition to the decline in the basal metabolic rate and the gain in weight, the patient shows a decline in his pulse rate and a gain in his physical strength and develops a sense of well-being. He comes to surgery in an excellent condition and usually tolerates the surgery without any noticeable change in pulse rate or blood pressure.

Diethyl Thiobarbituric Acid (Thiobarbital)

The third manner of treatment involves the utilization of diethyl thiobarbituric acid. The effects of this drug in animals and clinically have been studied by Astwood,[10] who reports that this drug exhibits a definite antithyroid effect. In lower doses it appears to exhibit more active antithyroid effect than does thiouracil, but at higher dosage levels it appears to be slightly less active than comparable doses of thiouracil. Satisfactory antithyroid effects have been obtained from the use of as little as 50 to 100 mg. of diethyl thiobarbituric acid daily. Preliminary clinical studies indicate that a dose of more than 100 mg. will rarely be required for control of even severe cases of hyperthyroidism. It is suggested that the treatment be inaugurated with a dosage of 50 mg. daily, and that this

may be increased to 100 mg. per day in severe cases. It is desirable that a total daily dose of 150 mg. not be exceeded. The daily dosage of the drug is usually administered in divided equal dosages and given at 8 to 12 hour intervals.

The drug has been of particular interest in the management of patients who are intolerant to thiouracil or thiourea. Several patients who could not tolerate thiouracil because of temperature reaction or skin rash have responded successfully to therapy with diethyl thiobarbituric acid. It is urged that the management of these patients be carefully controlled with repeated observations of the basal metabolic rate, pulse rate, and blood cholesterol. They should have observations of the red blood count, hemoglobin concentration, total differential white cell counts at the repeated intervals as executed in the use of thiouracil.

Prerequisites for Subtotal Thyroidectomy

It is necessary to choose a time for the operation when the patient's condition and clinical manifestations fit into a so-called remission. The methods of determination of operability are quite arbitrary and are subject to individual variation by different clinicians. It is for this reason that we will attempt to set out certain specific criteria in estimating the clinical condition of the patient for the proposed surgery. The points outlined below coincide closely with those advocated by Cole.[11]

A. Gain in Weight. This is the most important single requirement in determining the ability of the patient to undergo surgery. The severely toxic thyroid patient should never be submitted to thyroidectomy when he has failed to show a distinct weight gain. There is no iron-clad rule as to the amount of weight an individual should have gained. However, the patient who is obviously malnourished and markedly underweight should show a greater increase in weight than a patient who has lost only a few pounds. In addition to the gain in weight, the patient manifests a gain in strength and he will indicate that he can climb more steps without tiring or can walk a greater distance with ease than before receiving medication. This gain in strength is associated with a sense of well-being by the patient.

B. Pulse Rate. In patients who are receiving treatment with Lugol's solution, the pulse rate should show a decrease to a level of 110 or below and those patients under thiouracil medication should show a decline in pulse rate to 100 or less. If the Lugolized patient develops a tachycardia of 130 or above on slight exercise or excitement, it is considered that the patient's toxicity is greater

and cardiac reserve lower than other signs may indicate; while a tachycardia of 110 or more with a patient under thiouracil medication under similar circumstances requires a closer evaluation of the patient's cardiac status.

C. Basal Metabolism Rate. The basal metabolism rate provides valuable information if taken in consideration with the other available data. Patients with a basal metabolic rate of over 50 after iodine therapy or patients with a basal metabolic rate of over 35 following thiouracil medication are likely to have considerable reaction following an operation. The surgeon must bear in mind that there is considerable variation in the performance of basal metabolism tests by different technicians and that the procedure is a difficult one to perform.

D. Response to Iodine or Thiouracil Therapy. There should be a definite decrease in the intensity of most of the symptoms such as nervousness, excessive sweating, sleeplessness, and weakness, and a distinct weight gain should be demonstrated. The patient receiving thiouracil will show a more marked reduction in his toxicity than a patient receiving iodine therapy. The clinical manifestations of hyperthyroidism will improve with a gain in weight, reduction in pulse rate, and a decline in the basal metabolism of the patient.

SUMMARY

The fundamental factors in preoperative management of the thyrotoxic patient include rest, high caloric diet, adequate intake of fluids, and administration of iodine or thiouracil. The greatest single factor in reducing the mortality rate of patients undergoing thyroidectomy has been the administration of iodine or thiouracil. Thiouracil should be reserved for moderate and severe cases of hyperthyroidism. It is important that associated complications such as diabetes and cardiac decompensation be controlled previous to surgery. The attainment of specific objectives in the preparation of hyperthyroid patients will assure a more uniformly safe conduct of the surgical procedure.

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PARENTERAL FLUIDS

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DURING the past two decades parenteral administration of fluids has become a routine practice and, unfortunately, many of the already known facts about water and salt metabolism have been ignored. Also, in recent years, other fluids suitable for parenteral administration have become available and other needs and uses have become known. It is the purpose of this paper to call attention to some of the basic biochemical and physiologic facts applicable to the administration of some of the commonly used fluids and to indicate usage in keeping with the physiologic needs of the patient.

In surgical patients parenteral fluids are generally given to maintain or to re-establish the following conditions:

1. Water balance
2. Electrolyte balance
3. Protein balance
4. Blood volume
5. Oxygen carrying power of blood
6. General nutrition

For those purposes the following commonly used fluids are available:

1. Glucose solution, 5 or 10 per cent.
2. Salt or electrolyte solutions—saline, Ringer's solution, Hartman's solution and M/6 sodium lactate solution.
3. Protein solution—amino acid mixtures.
4. Colloidal solutions—gum acacia, gelatin, and pectin.
5. Whole blood.
6. Blood plasma, serum or albumen.
7. Blood cell suspension.
8. Fat emulsion.

Water Balance

The water balance in health is a most perfect mechanism. This is obvious when one realizes that in spite of a very variable daily intake of fluid the daily weight of an individual changes very little.

A 10 per cent change in water content produces definite symptoms. Water is normally lost (1) by vaporization from the lungs and skin, (2) by urine excretion and (3) in the stool. Coller and Maddock[1] have stated that the basic requirements for a patient in bed are 1000 to 1500 c.c. for vaporization and a similar amount for urine excretion. Not more than 200 c.c. are lost in the stool. This makes a total required intake of 2000 to 3000 c.c. and this amount must, obviously, be increased in numerous disease conditions such as fever, thyrotoxicosis, and in hot weather. It is to be remembered that water for vaporization is used first, and a scanty, concentrated urine means inadequate water intake. Of course, still more water is required when there is vomiting, fistula drainage, diarrhea, etc., and electrolyte need is also acute.

Water intoxication is more likely when there is protein and/or electrolyte imbalance, but it is otherwise possible. A patient with a barely compensated heart may be thrown into decompensation by fluids given too rapidly or excessively. A patient may have kidneys that are able to excrete only a minimum quantity of water. Such patients are also unable to excrete salt in more than small quantities. When these abnormalities are disregarded and excessive water (or salt) is given, waterlogging of the tissues occurs. Even death from excessive water administration is reported.

Electrolyte Balance

As in water balance, the salt conserving mechanism of the body is very efficient. In spite of the large amount of salt-containing fluid poured into the intestine daily (8 to 10 liters) only about .2 Gm. salt is lost in the stool. This salt-containing fluid averages about .5 per cent sodium chloride, which is the chief electrolyte present. Except in extremes of exercise, heat, and humidity not much salt is lost through the skin. The kidney conserves salt in direct proportion to its need in the body. As little as .1 Gm. per day may be excreted when the intake is low. Also, the excretion is on the basis of individual ions and the kidney is a good selector of those ions needed for retention and those for excretion.

In certain disease conditions there is excessive salt loss and replacement is necessary. Acid-base equilibrium must also be maintained. In vomiting due to pyloric obstruction chloride ions are lost in excess of sodium ions and alkalosis results. Plasma (or blood) chloride is low and carbon dioxide combining power is high. In gastric siphonage both acid and base are lost. In intestinal obstruction, particularly when high, this is especially great. There is a marked lowering of chlorides but carbon dioxide combining power remains about normal. The total base, however, is low. In biliary

or pancreatic fistulas the drainage is alkaline and a relative acidosis occurs. CO_2 combining power is low and chlorides are low. Ileostomy drainage presents a similar disturbance in blood chemistry. Diarrhea causes the greatest loss of base and Hartman's solution may be used advantageously in its treatment because it provides extra base in the form of sodium lactate.

It would seem that correction of these conditions would present a hopeless confusion, but such is not true chiefly because of the selective mechanism of the kidney. Because of this mechanism, isotonic saline, Ringer's solution or Hartman's solution will correct any of these electrolyte abnormalities provided sufficient water (as dextrose solution) is given. The kidney retains the sodium or chloride ion as needed and excretes the excess ion.

It is pertinent to point out that salt is often given without due regard for its need. In ordinary instances, that is, the absence of abnormal body fluid loss, very little salt is required—probably not over 5 Gm. daily. Fortunately, normal kidneys can excrete large amounts, if adequate water is given, and usually no harm results from excessive salt intake. However, in such cases, the kidneys are unduly loaded. That excessive salt may do harm in some patients was pointed out as early as 1913 by Trout[2] and again in 1924 by Matas.[3] Sick patients, surgical or medical, frequently have enough kidney damage to make any additional load very hazardous. Under such conditions salt may be retained and water, too, is held by the tissues, and edema results. This phenomenon is especially likely to occur if, as is true in many surgical patients, there is a low level of tissue proteins. Coller[4] has recorded definite clinical evidences of salt intolerance such as weakness, disorientation, anorexia, nausea and vomiting, distension, oliguria and edema. These symptoms disappear when necessary measures against salt retention are taken. It is well to remember that these conditions may prevail especially in the presence of a low plasma chloride.

This all seems confusing, but it serves to indicate that salt solutions should be administered, not empirically, but for a definite purpose and with an understanding of the physiologic needs of the patient.

What then is the practical and proper manner of correction of water and salt deficiencies? First, the oral route should be used, if possible. Otherwise some parenteral route is necessary. If the patient is not losing fluid in some abnormal manner, the principal need is for water to replace that lost by vaporization and to maintain an adequate urinary output. This is best accomplished by giv-

ing 5 per cent glucose in amount sufficient to maintain a urine volume of 800 to 1000 c.c. and will require about 2500 c.c. daily. Five per cent glucose is 98 per cent utilized by a nondiabetic, if given at the rate of 300 to 500 c.c. per hour. As much as 4000 c.c. or more may be required daily, if the weather is hot or if the patient has fever, a high basal metabolic rate, etc. If heart disease or nephritis is present, there must be due regard for them. In the usual surgical patient, provided there has been no excessive fluid lost by perspiration, hemorrhage, etc., no saline need be given postoperatively for the first day or two and then not more than 1000 c.c. normal saline (9 Gm. sodium chloride) per day. But, when the patient is losing body fluid by vomiting, gastric suction, fistula drainage, diarrhea, etc., quantitative replacement should be made with equal amounts of saline (or Ringer's) and 5 per cent glucose in addition to giving enough 5 per cent glucose to maintain a reasonable urine output. *Salt should be given for a definite purpose and never as a routine.* In addition to salt and water needs, other physiochemical needs become apparent which will be discussed in succeeding paragraphs.

Protein Deficiency

The plasma proteins, of which albumen is the principal factor, serve to maintain the osmotic pressure of the blood. This just equals the capillary pressure and any break in the balance results in edema (Starling's hypothesis). Three types of protein deficiency, or, more accurately, hypoalbuminemia, exist.

1. Acute, resulting from such conditions as acute hemorrhage, severe tissue trauma, and burns. Blalock[5] has shown that plasma fluid loss alone in such conditions is sufficient to produce the symptoms of shock.

2. Subacute, resulting from such conditions as peritonitis and intestinal obstruction.

3. Chronic, as noted in nutritional deficiency, chronic blood loss, nephrosis, chronic liver disease.

In the acute and subacute types, shock is a prominent feature and exists in proportion to the plasma loss. Hemoconcentration is evident in burns, peritonitis and intestinal obstruction. Other manifestations are abdominal distension due to edematous viscera, excess liquid in the lumen of the viscera and even extraluminal liquid (ascites and pleural effusion). Edema of the body and extremities is a late occurrence. Faulty wound healing is also notable.

Blood chemistry studies aid in the estimation of protein deficiencies but the plasma protein values are open to errors of inter-

pretation. The albumen-globulin ratio must be known and the degree of hydration is important. The unit volume value may be normal even though the total amount may be greatly decreased. This error can be corrected by application of the hematocrit reading.

Correction of hypoproteinemia is not easy. In the acute form correction is less difficult because the tissue proteins are not greatly depleted. Plasma, serum or albumen in the necessary amounts will correct acute protein loss. The cell volume, hemoglobin or cell count are means of gauging the dosage. A good plan is to keep the red cell count at a value below 6,000,000. Burns may require very large amounts. Recent information suggests replacement with considerable quantities of whole blood in order to prevent subsequent anemia in burns. If there has been whole blood loss, as in hemorrhage, only whole blood can replace it.

In the chronic form of hypoproteinemia, protein replacement by parenteral means is extremely difficult. This is easily understood when one realizes that to add 1 Gm. protein to the plasma an additional 30 Gm. are required for the tissues. To correct even mild chronic hypoproteinemia would require fantastic amounts of plasma. This is possible, however, in babies, because of their small weight, with plasma alone. Certain amino acid and protein hydrolysate (amigen) preparations are available and offer real promise. The latter preparation, according to Elman and Lischer,[6] is capable of supporting growth, maintaining nitrogen balance and even raising plasma proteins. It would seem to be of real value in all types of chronic hypoproteinemia and possibly helpful in the acute forms. Amigen is best given in 5 per cent concentration in 5 per cent glucose. The reactions are few and rarely severe. About the maximum amount that can be given safely is 25 Gm. per hour. In the subacute forms it would seem that a combination of plasma and amino acids might be useful. It is to be remembered that in such conditions as fistula drainage, burns, peritonitis and intestinal obstruction, water and salt balance must also be maintained as previously indicated.

Blood Volume

According to Blalock,[5] diminished circulating blood volume is the principal factor in traumatic shock. This is true whether the shock is due to hemorrhage, trauma to muscle masses, intestinal trauma, burns, peritonitis, intestinal obstruction, etc. In mild cases the tissues give up fluid to the blood stream and compensation occurs. Administration of crystalloid solutions will also furnish adequate fluid. But in more severe shock (greater decrease in blood volume)

such solutions are not adequate. Excessive crystalloid solutions may even be harmful because protein is washed out through excessively permeable capillaries. As a result of this observation attempts have been made to use colloidal solutions on the assumption that colloids would be held in the blood stream. Such solutions as acacia, however, have not proved safe and probably had best not be used. Obviously, then, only whole blood, plasma, serum or albumen will serve the purpose. In hemorrhage, plasma is of temporary aid but only blood cells can correct the deficiency in oxygen carrying power.

Oxygen Carrying Power of Blood

This function is possible through the hemoglobin in the red cells. Anoxemia is an important factor in shock and is increased when the amount of hemoglobin falls below the critical level. It is a factor in the production of increased capillary permeability. As stated above, only whole blood will be adequate in hemorrhage and must be given before irreparable damage has been done. Red cell suspensions may prove valuable in certain types of anemia where hypoproteinemia is not so great a factor.

General Nutrition

Complete parenteral feeding is rarely desirable but it has been done by the pediatritians for short periods of time. Helfrick and Abelson[7] report parenteral administration of all food elements of adequate and balanced caloric value. Glucose, amino acids and fat emulsion were used.

Summary

1. Parenteral fluid administration is an extremely valuable procedure but should be done in a physiologic manner.

2. When water is needed it should be given as 5 per cent or 10 per cent glucose in amounts of 2000 to 4000 c.c. daily, the determining factor being an adequate urine output.

3. Saline or other electrolyte solutions should not be ordered routinely but should be given in amounts just adequate to replace losses. The ordinary surgical patient, unless there is abnormal loss of body fluids, does not need saline during the first day or two. Acidosis and alkalosis can be corrected with saline (or Ringer's or Hartman's solutions) in the presence of normal kidneys if enough water is given for excretion of the excess ion.

4. Crystalloid solutions should be given only with great care in severe shock because of the "washing out" effect.

5. Hypoproteinemia of the acute or subacute form is best cor-

rected with whole blood and/or plasma. Chronic protein deficiency can be at least partially corrected with amigen. Parenteral protein administration can be counted on to become as commonplace as, and certainly as important as, the administration of glucose and saline solutions. The ideal protein solution, however, is not yet available.

6. Blood alone will correct the results of hemorrhage. Red cell suspensions may prove useful in anemias of certain type.

7. Complete parenteral feeding of all elements is possible.

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LIPOMA OF THE COLON

Treated by Primary Resection, with End-to-End Anastomosis

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IN 1906 Dewis[1] reported 44 intestinal lipomas. Their locations throughout the gastrointestinal tract were as follows: duodenum 6, jejunum 4, ileum 7, cecum 2, colon 5, sigmoid 5, rectum 6, small intestine 2, unlocated 1. Intussusception was present in 16 of these.

Stetten[2] in 1909 reviewed the literature concerning lipoma of the entire intestinal tract and added 2 cases. Numerous other reports have appeared from time to time. Pemberton and McCormack in 1937[3] reported 113 cases of submucous lipoma of the colon and rectum appearing in the literature up to that time. The tumor presented symptoms in 94 of these cases. They added 3 cases in which an exteriorization type of resection successfully corrected the condition. Many show varying degrees of intussusception. Lazarus and Marks[4] stressed this symptom in a paper entitled "Submucous Lipomas of Colon with Special Reference to Acute and Chronic Intussusception."

In a recent paper on surgery of the colon[5] one of us (JMM) advocated in elective, non-obstructive, prepared cases, where resection of the large intestine is indicated, that an aseptic, primary, end-to-end anastomosis be performed with the use of the Stone clamps.[6]

The following report of a submucous lipoma of the splenic flexure of the colon is of interest because of the relative rarity of the condition. It also serves to demonstrate the technic just mentioned.

R. S. M., a white female, married, age 65, was first seen by Dr. Julius Linn, April 15, 1946, with the complaints of constipation of 4 months' duration, mucus in stools of 6 weeks' duration, slight blood streaking of stools of 3 weeks' duration, and aching pain in the left upper quadrant of 4 weeks' duration. The general physical examination was essentially negative. No mass could be felt, nor was there any tenderness. Sigmoidoscopic examination was negative. A filling defect in the splenic flexure was visualized by barium enema (fig. 1).

The patient was admitted to the hospital April 20 and was placed on a high calory, low residue diet. For the first 48 hours she received enemas and laxatives, after which succinylsulfathiazole was given as follows: initial dose,

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16 Gm., followed by 5 Gm. every 6 hours. This dosage was calculated according to the recommendations of Poth.[7,8,9] The drug was administered up

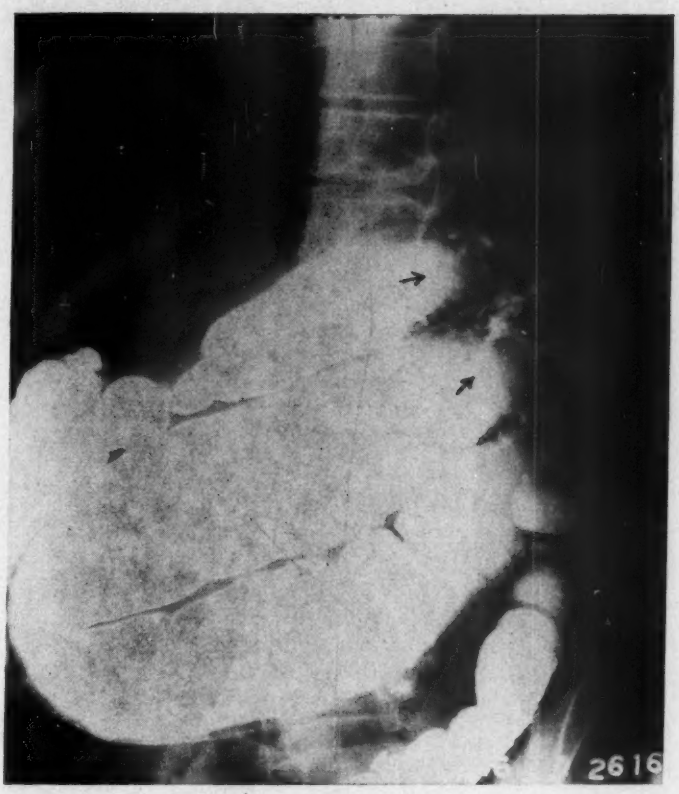

Fig. 1

to the time of operation and was resumed 48 hours after operation and continued for one week.

Operation: On April 26, under spinal anesthesia supplemented by sodium pentothal, a left rectus incision was made. The splenic flexure was mobilized and brought out on the abdomen. The mass in the colon was at first thought to be a polyp. It was obvious that it was not a napkin-ring carcinoma, which had been suspected before the operation. The tumor was causing a mild degree of intussusception and this intermittent obstruction was the cause of her pain. On gross examination after removal the specimen was found to be a lipoma with ulceration of the mucosal surface (fig. 2).

As is usually found following the use of succinylsulfathiazole the intestines were empty of feces and gas and in good condition for a primary resection. This was carried out with end-to-end anastomosis over Stone intestinal clamps (fig. 3, 4, 5, 6, 7).

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The patient stood the procedure well. She was given 1000 c.c. of 5 per cent glucose and 500 c.c. of blood during the operation. The postoperative course was quite smooth and uneventful. The Levine tube which had been placed in the stomach before the operation was left in situ during surgery and was removed 48 hours later. There was never any abdominal distention or vomiting. On the fourth postoperative day the patient passed gas by rectum and on the fifth day spontaneous bowel movement occurred. It was not necessary to give enemas. The wound healed per primum.

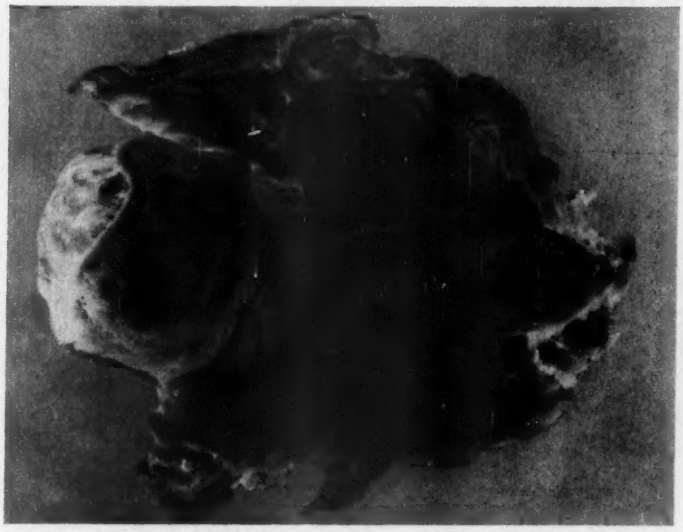


Fig. 2

The patient was allowed out of bed on the 11th postoperative day and was discharged on the 14th postoperative day. A check-up at the end of 3 months showed her to be quite well.

Pathologic Examination and Report: The specimen consists of a portion of resected colon. On the peritoneal surface there is a slightly protuberant mass 2 cm. in length and width and just slightly elevated above the peritoneal surface. When the bowel is opened a polypoid tumor is found projecting into the lumen. This is approximately 5 cm. in length and 3.5 cm. in width and thickness. The tip of it is ulcerated, reddish, and covered with exudate. The remainder of the surface is covered by normal large bowel mucous membrane. On section the central portion of the polypoid mass is made up entirely of lobulated yellow fat.

Diagnosis: submucous lipoma with superficial mucosal ulceration.

Technic of Aseptic Intestinal Anastomosis With Use of Stone Clamps

STEP 1. Tumor is isolated and area of colon to be resected is freely mobilized.

STEP 2. The epiploic appendices are carefully removed from area to be transsected in order to provide a smooth peritoneal surface for suturing.

STEP 3. Crushing clamps are placed across the lumen of the colon to be

resected and Stone clamps are applied to the ends to be anastomosed. Transection is done with the actual cautery, the crushing clamps coming away with

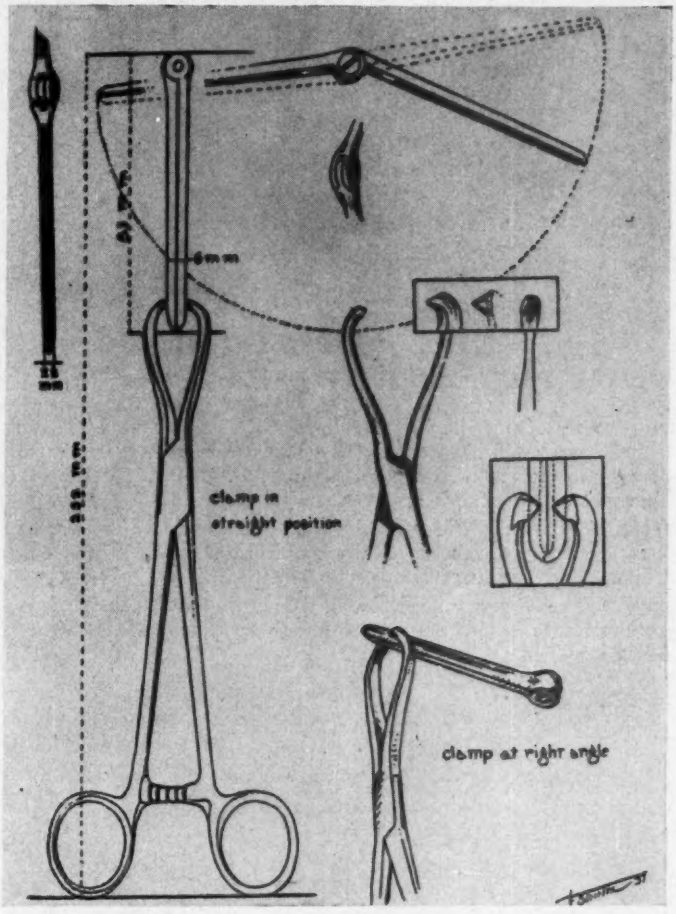


Fig. 3. Details of the Clamp, with dimensions and positions.

the tumor; the Stone clamps remaining attached to the resected ends of the colon.

STEP 4. The Stone clamps are approximated as shown in Figure 5, and the posterior line of sutures is placed. Interruptured Lembert sutures of fine silk are inserted and tied. The end sutures are left long to serve as guides. As has been emphasized by Dr. Halsted,[10] it is important that these sutures include the submucosa. This layer of the intestine contains fibrous tissue and lends the necessary strength to all types of intestinal anastomoses.

STEP 5. The Stone clamps are now brought together and are made to touch as shown in Figure 6. The anterior row of sutures is then placed; interrupted

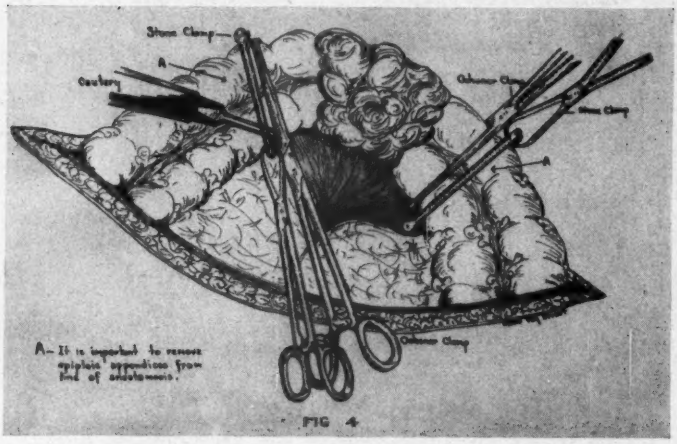


FIG 4

mattress sutures of fine silk being employed. These are left untied until all are placed. They are held taut as the Stone clamps are removed and are drawn more snugly to prevent the escape of gas or feces. The sutures are then tied. Thus an aseptic anastomosis has been performed.

STEP 6. As shown in Figure 6, the corners and both the anterior and posterior suture lines are reinforced where necessary, and all raw surfaces are inverted with interruptured Lembert or mattress sutures.

STEP 7. Figure 7 shows the closure of the rent in the mesentery. It is of the utmost importance in this step not to injure any blood vessels which supply the resected ends of the bowel.

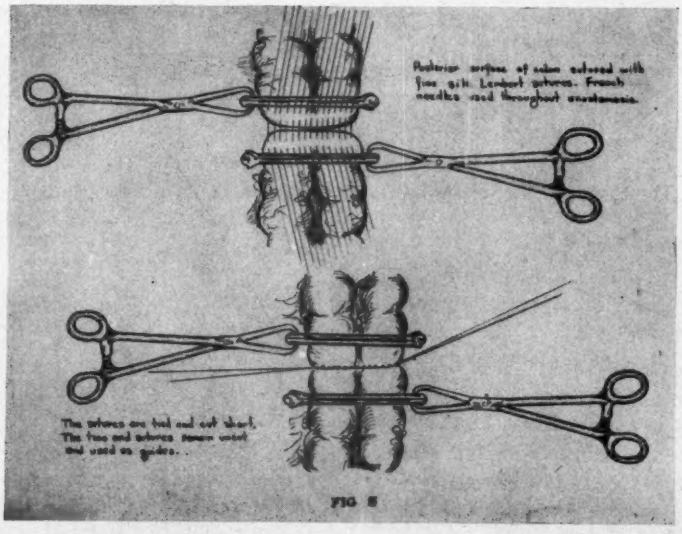
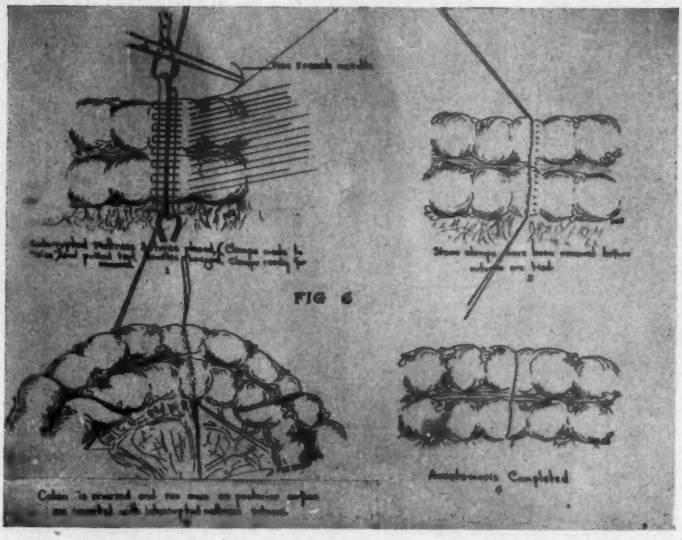

Posterior surface of suture covered with
fine silk Lembert sutures. French
needles used throughout anastomosis.
The sutures are tied and cut short.
The free end sutures remain uncut
and used as guides.

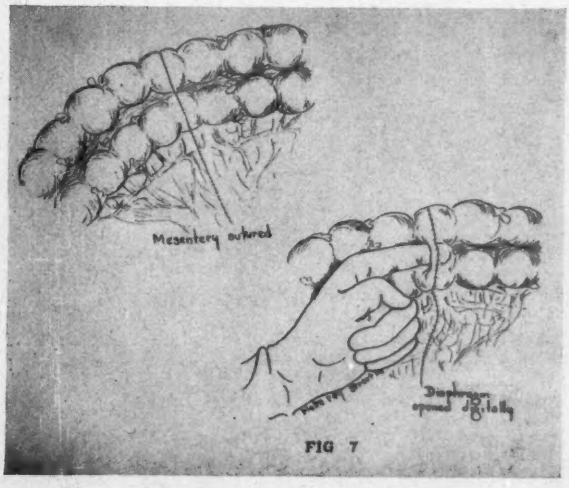
FIG 5



STEP 8. Finally, one tests the patency of the stoma by digital examination, breaking through any diaphragm which may have resulted from the crushing effect of the clamps.

SUMMARY

1. Four references are made to the literature on lipomas of the intestinal tract.



2. A case of submucous lipoma of the splenic flexure of the colon is reported.

3. A technic of aseptic, end-to-end anastomosis, using the Stone intestinal clamps is described and illustrated.

Conclusions

1. Lipomas are found throughout the intestinal tract.

2. They may be subserous or submucous; the latter are considered true lipomas.

3. They may be asymptomatic when small or may cause symptoms.

4. Where symptoms are present they are often due to varying degrees of intussusception.

5. Preparation of the colon with succinylsulfathiozale followed by resection and primary, end-to-end, aseptic, anastomosis using the Stone intestinal clamps is a satisfactory method of treatment. This technic when feasible presents obvious advantages over the two stage exteriorization type which requires more prolonged hospitalization and operation for secondary closure.

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REPAIR OF INGUINAL HERNIA WITH WHOLE SKIN GRAFTS

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OUR interest in the use of whole thickness skin grafts for hernia repair was stimulated by a report of George B. Mair,[1] of Aberdeen, Scotland. In 1938, Mair successfully repaired a large ventral hernia by the use of an implanted whole skin graft excised from the redundant skin over the hernia. Between 1938 and 1943, he used a similar method of repair on 7 large ventral, 3 umbilical and 1 epigastric hernia. A total of 119 inguinal hernias, direct, indirect and recurrent, were also repaired by this method. From a total of 137 cases the complications reported were sepsis in 2 cases which cleared in 21 to 28 days, 7 mild cases of bronchitis and one scrotal hematoma, which cleared. We were impressed with this type of repair which seemed to afford the best anatomic barrier and physiologic repair so far used for correction of hernias. In order to prove to ourselves the efficacy of this type of repair we chose 6 inguinal hernias for application of this technic. The experimental use of whole skin graft implantation was purposefully confined to the inguinal type of hernia. This is a smaller type of hernia and requires less skin than a large abdominal hernia would require. Although these have been successful in Mair's hands we felt it would be safer to apply a new technic in simple operations. We plan later to apply this type of repair in more formidable hernias.

This is a preliminary report of the successful repair of 6 inguinal hernias by the use of whole thickness skin grafts. The grafts were excised from the abdominal wall over the hernia site and implanted over the floor of the inguinal canal. The first repair was done one year ago and the last one two months ago. Six male patients, varying in age from 18 to 54, who agreed to this type of repair were chosen. The types of inguinal hernias repaired included three indirect inguinal hernias, one direct inguinal hernia, one sliding hernia of an indirect type, and one recurrent saddle bag type hernia following a previous modified Bassini repair three and one-half years previously. Sutures were removed on the 7th to the 9th day. Movements were restricted for the first 10 days and all patients were discharged between the 10th and the 15th postoperative day by am-

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bulance. Movements out of bed were not allowed until the 18th to 20th day. The only immediate postoperative complication was bronchitis which developed in one case on the second postoperative day and cleared up in two days. All cases were free from wound infection. The time interval is not sufficient for proper evaluation of recurrence rate. To date there has been no recurrence or late postoperative complications.

Operative Technic

The technic used closely followed that described by Mair. A few minor variations were made, which will be described later. We would recommend his article for a more detailed description of technic than this paper will afford.

The patient was given a tub bath and his abdomen and pubic areas thoroughly shaved, scrubbed with soap and water for 10 minutes, cleansed with ether followed by an alcohol and merthiolate application. This area was covered with a thick alcohol compress and a sterile towel was taped in place. This procedure was repeated once every 24 hours for three days preoperatively. At the time of operation skin cultures were taken from the area to be used for grafting.

The skin incision was made in the usual inguinal region and a piece of elliptical whole skin was removed from the upper pole of the incision about two inches long and one inch wide. The upper part of the incision was chosen in preference to removing the skin from over the pubic area which potentially would harbor more bacteria. The elliptical piece of skin removed was denuded of all fat and subcutaneous tissue and placed in saline.

The external oblique fascia was incised, the cord was dissected free, the hernial sac was exposed and removed in the usual manner. The internal ring was tightened by a suture above and below the ring in the transversalis fascia.

The elliptical piece of excised skin was then prepared by cutting across each end about ¼ inch to allow for a more rectangular shape. One end of the skin was split for about ½ inch, to be used to form a new internal ring. The opposite extremity was anchored by three sutures to the lower anterior aspect of the rectus sheath, the fascia over the symphysis pubis and the extreme medial edge of the Poupart's ligament. The lateral edge of the skin graft was sutured to the shelving portion of the Poupart's ligament and the medial edge was sutured to the rectus sheath. The sutures fixing the skin graft were placed about a quarter of an inch apart. Extreme care was taken to stretch the skin taut and to suture it under tension.

We would like to emphasize the importance which Mair attaches to placing the skin graft under tension. This accomplishes two things, (1) the inguinal floor is in close apposition to the inferior surface of the graft, thus avoiding a dead space beneath the graft; (2) the epidermis cannot overlap thus allowing later cyst formation. Zimches[2] found in experiments on dogs that a buried whole thickness skin graft implant will fold on itself in a U formation and form a closed cystic cavity lined with epithelium.

The pedicles which have been formed by splitting the upper extremity of the skin graft were then placed around the cord at the level of the internal ring. The pedicles were joined superior to the internal ring and care was taken that the ring was not too tight. Thus a complete barrier was placed in the floor of the inguinal canal beneath the cord to prevent any direct recurrence. A second internal ring was created medial and superior to the reinforced internal ring as a second barrier to an indirect recurrence.

Mair recommends thirty-day chromicized catgut for this repair. In five of our cases No. 1 chromic catgut was used. In one case black silk was used and this was found very satisfactory. We feel that black silk or cotton is probably the better suture as it requires a smaller needle and there is less tissue reaction with a non-absorbable suture.

The external oblique fascia was closed over the cord with interrupted sutures. Camper's and Scarpa's fascia were approximated. The skin was closed with interrupted black silk inverted mattress sutures. This closure is not difficult and leaves a hockey stick shape wound. Mair points out that this type of incision is reputed to be kept more readily free from infection, to facilitate dressing and to be more comfortable to the patient. A firm compression bandage was applied.

We prefer a low spinal anesthesia and this was used without supplement in our six cases. Ten to fifteen milligrams of pontocaine was found to be sufficient to give good muscular relaxation at the time the skin graft is sutured in place in order that the tension on the graft will increase with the return of muscular tone.

Discussion of Contraindications

At the present time we do not believe that there are any more contraindications to this type of hernia repair than there would be to the more commonly used types of repair.

The two most frequent criticisms made of this technic have been (1) the added risk of infection; (2) the danger of epidermoid cyst

formation. The first of these criticisms, the added risk of carrying infection into the wound, can be minimized by the proper preparation of the skin to be used for the graft. We had no sepsis in our cases. Four of the skin cultures taken at operation were negative for bacterial growth. One was positive for non-hemolytic staphylococcus. One culture taken by the swab method was positive for hemolytic staphylococcus albus but the plate where the skin was directly applied to the agar was negative, therefore we felt that this was a contamination. Mair reported only two cases with sepsis out of his total of 137 hernias repaired by this method. This is a very low percentage and compares favorably with that of any widely used surgical procedure.

In reference to the second criticism, the formation of an epidermoid cyst, Mair had an opportunity to explore an inguinal repair in which the whole skin graft had been used three months after operation. The graft was firmly attached and he found it impossible to identify where the graft ended and normal tissue began. There was a close resemblance of the graft to the tissue to which it was sutured. A section was removed and the histology was that of a highly vascular connective tissue in which dermal or epidermal elements could not be identified. The graft was richly infiltrated with collagenous fibers and there was firm adhesion to the underlying muscle. There was no trace of even microscopic cyst formation, but a number of giant cells were observed. The work of Uihlein[3] on sections of the cutis graft used in humans showed a complete metamorphosis of the transplant. The graft represented normal connective tissue with its fibrous and fatty components, blood vessels and nerves. No hair, pilonidal follicles or glandular tissue could be identified and there was no evidence of cyst formation, by either gross or microscopic examination.

Summary

1. Six inguinal hernias repaired by whole thickness skin grafts by the Mair technic are herein reported.

2. The operative technic has been discussed and certain minor changes have been recommended.

3. Wound sepsis did not occur in any of the 6 cases.

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INTRACRANIAL ANEURYSMS: CONSIDERATIONS IN SURGICAL MANAGEMENT

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Intracranial aneurysms have been the subject of clinico-pathologic reports for many years. As evidence of the frequency of this condition McDonald and Korb[1] in a comprehensive review of the literature summarized over 1,000 cases prior to 1939. The high mortality in this condition is attested by the fact that most of the reported cases include autopsy findings. In an excellent clinical and pathologic study Richardson and Hyland[2] reported a mortality of 50 per cent in the first episode, and diminishing mortality in each succeeding episode. Thus, while one may survive one or more hemorrhages, there is always the possibility of another, and fatal, hemorrhage.

It is evident that many statistical data regarding the percentage of cures and fatalities in subarachnoid hemorrhage are inaccurate because the follow-up span is not sufficient to ascertain whether the ultimate cause of death in every case reported as cured actually is independent of the intracranial aneurysm. We have recently observed an autopsy in a patient who had a sudden fatal rupture of an aneurysm ten years after a single episode of subarachnoid bleeding. Such a case might well have been termed a "cure" until the moment of fatal rupture.

Etiology

The relative prevalence of aneurysm of the intracranial vascular tree is doubtless related to the mode of embryologic development of the circulus arteriosus and its branches. The currently accepted view regarding the lack of proper development of the media of the arterial wall at points of bifurcation may well explain miliary aneurysms in these locations.[3] Many aneurysms, however, occur where there is no branching. These anomalies are probably due to the persistence of rudimentary embryonic branches and anastomoses. That age is no factor in the development of aneurysm is shown by the fact that these lesions are found in every age group, from early childhood to senility.

Pathology

As these lesions are frequently anomalous in development there is later a combined picture of abnormal formation with superim-

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posed arteriosclerosis and necrosis of the aneurysm wall to account for the fatal rupture.[4] This may of course occur in the absence of any evidence of generalized vascular disease. Aneurysms have been reported due to syphilis, rheumatic fever,[5] acute infections and septicemia. The mechanism of production of the aneurysm is a local arteritis with later weakening of the wall and saccular dilatation of the vessel.

Vascular hypertension does not bear any direct relationship either to the development of aneurysms or to their rupture. What is more important in the precipitation of rupture of an aneurysm is not a sustained hypertension, but rather some sudden elevation of vascular tension beyond its accustomed range.

Symptomatology

There may be prodromal symptoms for a variable period before rupture. Headache, vertigo, visual disturbances, dementia and somnolence have been described. The symptoms of rupture are usually sudden in onset and consist of severe headache, coma, nuchal rigidity, fever and focal symptoms according to the location of the aneurysm and the hemorrhage. Visual disturbances due to pressure on the optic pathways are common.[6] Oculomotor palsy is frequently seen. Hemiplegia may be due to intracerebral extension of the hemorrhage. During recovery ataxic gait and mental symptoms may be manifest.

Diagnosis

Certain unruptured aneurysms produce characteristic syndromes, especially those of the internal carotid artery.[7] The 3rd and 5th cranial nerve changes localize the lesion well. After rupture the diagnosis is evident but the localization may be difficult. The monumental work of Moniz[8] opened the way to the solution of this difficult problem by angiography of the intracranial vessels. Occasionally an aneurysm will reveal its presence by curvilinear calcification in its wall which is visible in the x-ray films.

Treatment

The management of the acute rupture is directed toward relief of severe headache, reduction of intracranial pressure, and sedation to avoid irritability and excitement. Absolute rest and quiet is the keystone of successful treatment, as emphasized by Sands.[9]

The cure of the aneurysm may present a simple problem or an extremely difficult one. Occasionally there may be multiple aneurysms, making surgical cure practically impossible. Certain prin-

ciples have been found to be helpful in the approach to this problem. Preliminary digital carotid compression followed by angiography and carotid ligation, by degrees if necessary, is an important prelude to the direct surgical attack on the aneurysm. The following cases illustrate various problems in the management of intracranial aneurysms.

Case Reports

Case 1. W. M. P., white male, married, age 51 years, was admitted to Jefferson-Hillman Hospital Aug. 18, 1946, in a delirious state, having developed a severe occipital headache while walking 24 hours previously. Eighteen hours later he lapsed into coma and had two generalized seizures. On examination he was found to be comatose, and with a divergent stabismus. The right pupil was widely dilated. Blood pressure 110/70. Pulse 68. Respiration 18. Temperature 100.2. There was nuchal rigidity. General physical examination was otherwise not remarkable. Laboratory: R.B.C. 4,410,000, Hb. 13.5 Gm., W.B.C. 19,000, Lymphs 5, Monos 2, Segs 90, Stabs 3, Eos 0, Bas 0, N.P.N. 30 mg. Urinalysis normal. Lumbar puncture, 8-18-46: initial pressure 310 mm., fluid grossly bloody; 10 c.c. slowly removed; final pressure 200. Lumbar puncture, 8-22-46: initial pressure 410, blood tinged and xanthochromic; final pressure 210. On August 25, temperature, pulse, and respiration were normal, the patient completely rational. He had no headache.

After discharge from the hospital he developed constant right supraorbital pain, dizziness, unsteady gait, and ptosis of the right eyelid.

He was readmitted on September 30 with above complaints. On examination he was found to have a right oculomotor palsy. His blood pressure was 136/90. Compression of the right common carotid artery repeatedly resulted in paresthesias in his left hand and arm after 7 or 8 minutes' compression.

Operation: On October 2, the right internal carotid artery was exposed in the neck. A diodrast injection was performed, after which the artery was partially occluded (estimated 50 per cent) by a tantalum band. He experienced immediate relief of right supraorbital pain, but his condition remained otherwise unchanged. He was discharged on October 7.

On November 1 he noted some recurrence of right frontal headache, which has become more severe recently.

Readmission Note: November 6, under local anesthsia, the right internal carotid artery was re-exposed and completely occluded by a tantalum band. He experienced no difficulty after this procedure, and was discharged on November 10, completely relieved of headache, supraorbital pain and dizziness. The right oculomotor palsy persisted.

Comment

This is a straightforward case of aneurysm of the intracranial portion of the internal carotid artery. The angiogram demonstrated the lesion (fig. 1). Because he would not tolerate complete occlusion of the internal carotid artery it was necessary to do the ligation gradually. This has relieved the symptoms but cannot be considered to constitute a cure of the aneurysm. This will be ac-

Fig. 1. Aneurysm of the supraclinoid portion of the right internal carotid artery, Case 1.

complished only by complete obliteration of the blood supply to the aneurysm through the circle of Willis. The intracranial operation for "trapping" the aneurysm distally is planned and will be carried out in the near future.

CASE 2. O. J. H., married white male, age 22 years, was admitted to the Employees' Hospital, Tennessee Coal, Iron and Railroad Company, on Jan. 18, 1946, complaining of severe bitemporal headache of several hours' duration. Immediately after the onset of the headache he lost consciousness, but became rational 15 or 20 minutes later.

Past History: Left renal stone, left hydronephrosis. Usual childhood diseases.

Family History: Noncontributory.

Examination: The patient was in excruciating pain (headache). Temperature 100, blood pressure 116/58, pulse 70, respiration 16. General physical examination was not remarkable. The only abnormal neurologic findings were mental confusion and suggestive Babinski signs bilaterally. There was no nuchal rigidity. Laboratory studies: R.B.C. 4,500,000, W.B.C. 15,500, urinalysis negative. X-rays of the skull were negative.

Course: On January 19 he was definitely stuporous, with nuchal rigidity, absent abdominal reflexes and bilateral Babinski signs. A lumbar puncture revealed grossly bloody fluid under 450 mm. pressure. This was lowered to 200 mm. by slow removal of 15 c.c. fluid. After this procedure he was much less restless. He remained comatose until January 23, during which period

Fig. 2. Post-mortem angiogram in Case 2. Although the artery is incompletely visualized, the middle cerebral artery is visible, displaced upward by the temporal lobe hematoma. The sac of the ruptured aneurysm is visible arising from posterior portion of the sylvian artery in the region of the angular gyrus.

daily spinal drainage was performed. He then generally improved except for persisting headaches and diplopia.

On February 6 we saw this patient for the first time and made the following entry on his record.

This man has had one severe episode of subarachnoid bleeding from which he has partially recovered. It is likely that other episodes will follow. The residual neurologic signs (left N. VI. weakness, right-sided hemiparesis) suggest a left-sided aneurysm. Advise left carotid angiogram.

His progress was so satisfactory that the patient and his family demurred at the suggestion of angiography. Within several days he was ambulatory and was ready for discharge when, on February 13, at 5:00 A.M., he began screaming with pain in his head. Within a few minutes he became irrational and incontinent of urine. Gradually he became more stuporous. At 10:00 A.M. he was observed to have a dilated, fixed left pupil and a flaccid right hemiplegia, with stupor.

Operation: At 10:30 A.M. the left carotid artery was completely occluded by a tantalum band. Because of his precarious condition angiography was not done.

Following this procedure his vital signs remained satisfactory, but his neurologic signs persisted unchanged. On February 14 he was still comatose but was observed to move his right extremities at times. On the 15th he developed respiratory embarrassment with deepening coma and expired approximately 48 hours after carotid ligation.

Autopsy (limited to head): Scalp and calvarium are normal. The dura is tense. The brain surface shows reddish collection of subarachnoid blood. The left temporal lobe is swollen and extremely soft. One section is made through the brain in the horizontal plane, which shows a hematoma in the left temporal lobe 7.4 x 6.5 x 6 cm., surrounded by friable yellow necrotic brain tissue. Posteriorly the cavity of the hematoma communicates with the atrium of the left lateral ventricle. The ventricles contain fresh blood clot.

A section along the left sylvian artery shows a branch at the level of the angular gyrus which gives rise to a saccular aneurysm 2.8 cm. in diameter. This aneurysm lies beneath the pia and within the necrotic brain substance. From its deep side the hemorrhage has occurred through a dissecting opening.

Comment

This case illustrates the importance of doing the angiogram as early as possible after the initial hemorrhage. Direct surgical attack upon the aneurysm would have been feasible had its location been known. Exposure of the circle of Willis as the surgical approach to an aneurysm in the presence of a 3rd nerve paralysis is not a sound doctrine, as is well illustrated here, for a frontal approach would have disclosed neither the aneurysm nor its hemorrhage although the aneurysm itself was in an easily accessible surface location (fig. 2). It is difficult to determine whether an oculomotor palsy is due to direct pressure on the nerve by the aneurysm, or by temporal lobe herniation at the incisure. The differentiation can only be made when there is involvement of adjacent nerves (trigeminal pain and sensory loss) by direct pressure also. This point was demonstrated within a month in another patient who presented an oculomotor palsy with subarachnoid hemorrhage, and was found to have a large intracerebral hematoma in the temporal lobe due to a ruptured venous angioma. In this case, also, internal carotid ligation was unsuccessful in the presence of massive rupture of an anomaly of one of its branches.

Case 3. J. M., white single female, age 42 years, was admitted to Jefferson-Hillman Hospital April 9, 1946, with complaint of nervousness, irritability and crying spells. These symptoms represented the only residue of an episode of subarachnoid hemorrhage in September, 1945. At that time she had suffered a severe headache, following which she lost consciousness and remained comatose one week. Repeated spinal punctures yielded grossly bloody fluid. Pressure not recorded. With recovery from that episode she no longer had headache, but developed the symptoms mentioned above.

Past history and family history, noncontributory.

Examination: A moderately obese, middle-aged white female who does not appear ill. She is somewhat facetious, and is emotionally unstable, crying spontaneously at times. Blood pressure 174/102, pulse 84, respiration 16. General physical examination was not remarkable.

Neurologic Examination: Gait and station, coordination, muscular sys-

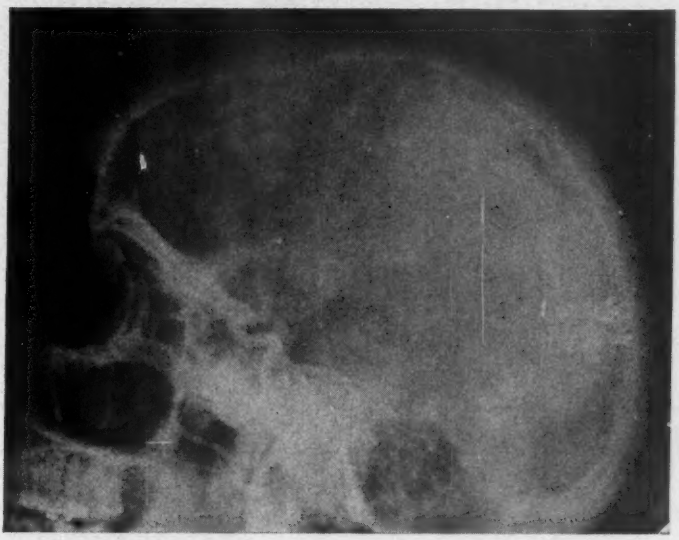

Fig. 3. Left internal carotid angiogram in Case 3, showing occlusion of the artery in the supraclinoid region, presumably by thrombus. The middle meningeal artery, which filled by reflux flow, is well visualized.

tem, and sensory system normal. Reflexes active and equal. No pathologic reflexes. Cranial nerves intact. Right handed.

Laboratory work: R.B.C. 4,520,000, Hb. 14 Gm., W.B.C. 8,350, urinalysis normal.

Operation: On April 10 a right anterior cervical incision was made and 15 c.c. of 35 per cent diodrast was injected into the exposed internal carotid artery.

X-ray report: Normal right internal carotid angiogram.

Course: She was discharged from the hospital on April 12 to return later for an injection of the left internal carotid artery.

Readmission Note: She returned to the hospital on May 19 with the same complaints and findings as noted on previous examination.

Operation: On May 21 a left internal carotid exposure was made in the neck and 15 c.c. of 35 per cent diodrast was injected. The internal carotid artery was then completely occluded by a tantalum band.

X-ray report: The left internal carotid artery is visualized up to its division into anterior and middle cerebral branches. No dye passes this point. There is reflux filling of the external carotid artery with good visualization of the middle meningeal artery throughout its course. The findings indicate thrombosis of the left internal carotid artery intracranially (fig. 3).

Course: She has continued to exhibit irritability and emotional instability. There has been no recurrence of headache or evidence of subrarachnoid bleeding.

Comment

This case was without objective localizing or lateralizing signs. Hence it was necessary to visualize both internal carotid arteries. The absence of headache after the hemorrhage, together with personality changes suggesting organic frontal lobe deterioration, probably indicate thrombosis of the aneurysm, with some resultant impairment of blood flow through the left frontal lobe. She tolerated complete occlusion of the left internal carotid artery by tantalum band with no difficulty, notwithstanding the fact that there had been no preliminary digital compression. This tends to confirm the evidence offered by the angiogram indicating that this artery was already occluded by thrombus.

Summary

Three representative cases are presented illustrating problems in management of intracranial aneurysms. In Case 1, the angiogram confirmed the clinical findings of an aneurysm of the internal carotid artery. The trapping of this aneurysm has been started. In Case 2, there was clinical evidence during rupture of an aneurysm of the circle of Willis on the left, but angiogram would have localized the lesion at another site and indicated the proper surgical approach, which otherwise might have failed to expose the aneurysm. In Case 3, the angiogram revealed thrombosis with spontaneous cure of the aneurysm; hence no surgery was necessary.

In three cases with massive hemorrhage the internal carotid artery has been occluded in the neck within 6 hours after the onset of coma. None of these patients survived. With present methods of treatment practically all of these cases of massive rupture expire in the first episode of bleeding. The only possible way to control hemorrhage of this magnitude is by exposure of the aneurysm or its main contributing artery intracranially. Although the patient is usually in extremis, this course offers little additional hazard when one considers the outlook in any such case.

Conclusions

1. Ruptured intracranial aneurysms present varied and individual problems in surgical management.

2. Carotid angiography is a useful procedure in planning the proper surgical management of these cases.

3. Internal carotid ligation in the neck is apparently not effective in controlling massive intracranial hemorrhage from a ruptured aneurysm of one of its branches.

4. Certain intracranial arterial aneurysms may be amenable to cure by surgery.

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MEDIASTINAL CYSTS

Report of a Case

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IN the past, mediastinal cysts have been mostly medical curiosities that have been found at the autopsy table. However, in recent years, since the rapid advance of thoracic surgery has been manifest, reports have occurred from time to time in which these cysts have been successfully removed.[1,2]

CLASSIFICATION OF CYSTS OF MEDIASTINUM

A. *Congenital*	*Derivation*
1. Epidermoid Cyst	Ectoderm
2. Dermoid Cyst	Ectoderm and Mesoderm
3. Teratoma	Ectoderm, Entoderm, Mesoderm
4. Pericardial CelomicCyst	Mesoderm
5. Bronchial Cyst	Mesoderm and Entoderm
6. Esophageal Cyst	Mesoderm and Entoderm
7. Gastro-enteric Cyst	
a. Gastric	Mesoderm and Entoderm
b. Enteric	Mesoderm and Entoderm

B. *Acquired*

1. Parasitic Cyst, caused by Taenia Echinococcus
2. Neoplastic Cyst, due to degeneration of hematoma

Eleven and four tenths per cent of the epidermoids, dermoids and teratomas are malignant. This group also comprises about 90 per cent of all mediastinal cysts. All of the other congenital cysts are benign.

Most of these cysts have given rise to symptoms during the first three decades. The most common symptoms are cough, pain in the chest, dyspnea, and hemoptysis.

Mediastinal cysts are usually visible as a smooth, round or ovoid mass that may be located in any portion. A very common location is beneath the carina and attached to the trachea or a main bronchus. If attached to the trachea or a main bronchus, it will move during the swallowing act. If attached to the esophagus, this can be determined by giving barium by mouth.

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Bronchogenic cysts are smooth and round. These may change over a period of time and may contain both air and fluid. Dermoids and teratomas are usually slightly lobulated and often contain calcified areas. These are usually found in the anterior mediastinum.

The following case report is presented:

Mrs. F. N., age 41, was admitted to the hospital on April 2, 1946, because of hemoptysis and pain in the left side of her chest for one month. The pain was severe enough to keep her awake. The hemoptysis consisted of blood-streaking. There had been no weight loss, fever or wheezing.

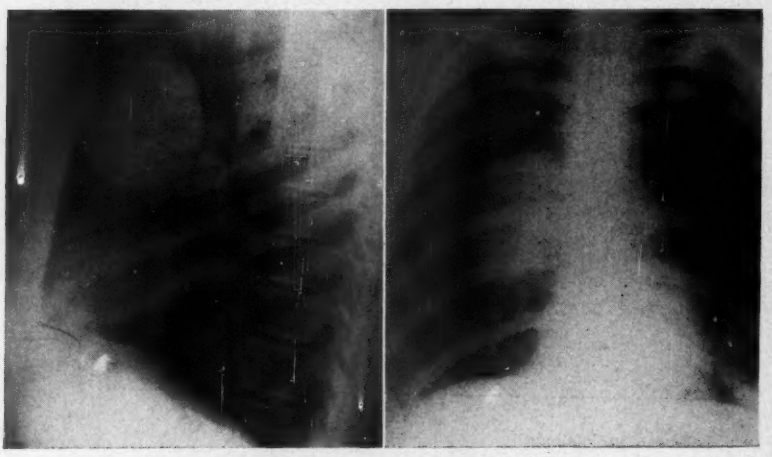
The patient stated that she had been admitted to a hospital in 1925, when she had a severe case of influenza. The patient also stated that she had had some vague discomfort in her chest for the past 20 years. X-ray of her chest at that time had revealed "something wrong with the chest." Several roentgenograms were made in 1925, and then the patient did not return.

Physical examination revealed a well-developed patient who was quite deaf. She was not acutely ill. The blood pressure was 120/80. The only abnormal physical findings were decreased breath sounds and dullness over the right anterior chest.

Roentgenograms revealed a well circumscribed mass in the right anterior mediastinum. Fluoroscopy revealed no pulsation. Flouroscopy and roentgenogram, made of the esophagus, revealed no displacement or involvement of it with this mass. The hemoglobin was 80 per cent and the leukocytes measured 8,000 per cubic millimeter. The erythrocytes numbered 4,200,000 per cubic millimeter. The Wassermann test for syphilis was negative. The urinalysis and electrocardiagram were normal. Bronchoscopy revealed a small amount of blood in the right main bronchus, with the architecture normal otherwise.

She was advised to have an exploratory thoracotomy, to which she consented after some delay. The operation was performed on May 9, under intratracheal cyclopropane anesthesia. A right anterior incision was made and the pleural cavity opened through the third interspace, and the third and fourth ribs were forcibly retracted with a rib spreader. Several fine adhesions between the right lung and the cyst were severed. The cyst arose from beneath the sternum, was non-expansile, and about the size of an orange. The mediastinal pleura over the cyst was freed by a combination of blunt and sharp dissection; in so doing, the mass was entered and a dark green, odorless fluid that had many yellow flecks of material came from the cyst. The mass was then found to extend behind the sternum to approximately one inch under the left cartilages. The left pleural cavity was also opened in removing the mass. The mass was then dissected from the ascending aorta and superior vena cava. It extended up and was most adherent behind the manubrium. The cyst was bound down with many adhesions. This dissection was carried out with considerable difficulty. All bleeding points were controlled with silk stick ties. The pleural cavity was washed out and a #18 catheter was left in the most dependent portion of the pleural cavity. Closure was with interrupted silk sutures. The postoperative condition was excellent. Other than having temperature 103 to 104 on the second and third postoperative days, her convalescence was uneventful. Recent roentgenograms (fig. 3) revealed her to have a good expansion of the lungs with no evidence of recurrence of the cyst. To date she has remained in excellent health.

The specimen was examined by Dr. J. A. Cunningham. *Gross:* Specimen consists of a large, ovoid, cystic mass 4 x 718 x 7 cm. It has an irregular surface with bits of fat tissue, lymph nodes and a fragment of mesothelium at-



Figs. 1 and 2. Lateral and Posteroanterior Views of the Chest Preoperatively.

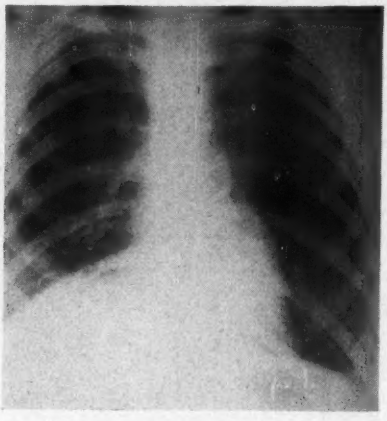


Fig. 3. Postoperative Roentgenogram.

tached to it. On section, it is a cystic mass with a wall 0.5 cm. thick. It has several separate cavities. The wall has a caseous-like substance with calcification occurring at intervals. The remainder of the wall is tough, fibrotic material. The lumen of the cyst is filled with thin, necrotic, caseous substance with calcific changes. The mass weighs 95 Gm.

Microscopic: Section through the specimen shows a dense, fibrous, tissue wall in which there are scattered fat cells and occasional lymphocytes. The lining of the cystic structure has been completely destroyed, and, in its place there are large numbers of needle-shaped cholesterol crystals with typical for-

eign body giant cells lined up around them. Some of these giant cells contain interesting typical asteroid bodies that one sees particularly in the interposition of muscle fragments. There are also numerous fat laden macrophages, as well as some macrophages containing hemosiderin. In some portions of the wall, there are focal collections of hemosiderin laden macrophages surrounded by moderate numbers of lymphocytes.

Diagnosis: Mediastinal cyst with cholesterol deposition, foreign body giant cell reaction, and evidence of old hemorrhage. (Four sections have been examined without demonstration of a specific lining. It is doubtful whether this can be demonstrated since the specimen is obviously old, having been in the body for some time.)

While it is impossible to say exactly what type of mediastinal cyst this is, there is a strong possibility that it is some type of embryoneal cyst, probably of the precardial celomic type.

Providing the patient is in good health, and below 50 years of age, mediastinal cysts, whether symptomatic or asymptomatic, should be removed, because if left alone they will sooner or later produce symptoms. The symptoms are caused either by pressure from enlargement, degeneration and infection, or by malignant changes.

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INTERNAL BILIARY FISTULAS

Report of a Case

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WHEN the gallbladder becomes infected, localization of the process is the general rule. The anatomic position of the gallbladder is such that acute inflammation in its walls quickly forms adhesions to surrounding organs. In those instances, in which obstruction to the cystic or common duct has occurred and acute infection prevails, parts of the extrahepatic biliary tree may become adherent to the surrounding organs and the stones may be discharged into the intestines or other viscera through spontaneous fistulous openings. These fistulas may also appear following rupture of a diseased gallbladder producing a pericholecystic abscess which secondarily necrotizes the intestinal wall; or by perforation of a viscus by an ulcer or carcinoma. If the fistula is small it may close spontaneously and the patient may receive sudden, prolonged, or even permanent relief from all symptoms. If the fistula remains open, reflux of intestinal contents into the biliary tree may lead to extensive cholangitis. It is the purpose of this paper to discuss internal biliary fistulas and to report a case in which a fistula developed between the colon and duodenum as a result of gallbladder disease causing extensive cirrhosis of the liver and producing unusual gastrointestinal symptoms.

FREQUENCY AND LOCATION

Spontaneous internal biliary fistulas, while not surgical curiosities, are very uncommon. In view of the high incidence of gallstones and gallbladder disease, their occurrence must be regarded as an unusual complication. In 1925 Judd and Burden[1] presented a study based on 153 cases of internal biliary fistula in which operation had been performed in the Mayo Clinic. In 1939, Wakefield and his associates[2] reported 176 cases of cholecystenteric fistulas which arose primarily from biliary disease. In a series of 10,866 routine necropsies, Roth, Schroeder and Schloth[3] found 43 biliary fistulas. Dean[4] reported 29 cases from the University of Iowa hospitals. There are other reports of smaller series in the literature. Many of these fistulas close spontaneously and are not found at the time of operation or necropsy.

Cholecystoduodenal fistulas are the more common type. In most

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instances the fistula leads from the fundus of the gallbladder but it may develop from the cystic or common duct. The gallbladder or bile ducts are usually closely attached to the intestine by adhesions; and intervening abscess cavities are rare. In the 153 cases reported by Judd and Burden[1] the fistula communicated with the duodenum in 117 instances, with the duodenum and colon in 4, with the stomach in 6, and with the colon in 26. In the 176 cases reported by Wakefield and his associates[2] the positions of the fistulas were as follows: between the gallbladder and duodenum in 101 cases; between the gallbladder and the colon in 33; and between the gallbladder and stomach in 7. Multiple fistulas between the gallbladder and adjacent organs and intestines were found in 11 patients. In these 11 instances the fistulas were usually situated between the gallbladder and the duodenum and liver. In 24 subjects the gallbladder had ruptured and the stones were discharged into the abdominal cavity.

Biliary calculi have been found in many unusual locations. Dean[4] states that gallstones have been found plugging the portal vein and hepatic artery; both men and women have passed gallstones in the urine; biliary calculi have been found with the placental membranes following labor; and the pleural and pericardial sacs have been invaded and forced to retain the contents of a diseased gallbladder. Wakefield and his associates[5] reported 10 cases of intestinal obstruction caused by gallstones, and there are numerous other reports of smaller series in the medical literature.

Symptomatology and Diagnosis

The usual history obtained from a patient with an internal biliary fistula is that of severe symptoms of disease of the biliary tract with colic, jaundice, chills and fever, followed by a period of comparative well-being after formation of the fistula. The formation of a communication between the biliary tract and the intestines is sometimes a lifesaving accident because it allows inflammatory debris and calculi to be spontaneously extruded from the biliary system and to be carried away with the feces. These fistulas frequently close unless the common duct is permanently occluded. Many instances of healed fistula are encountered at operation; the gallbladder being diseased, usually small and shrunken, containing foul bile, pus, and stones. If a fistula between the gallbladder and intestinal tract remains open, reflux of intestinal contents into the biliary tree may lead to extensive cholangitis and biliary cirrhosis of the liver, or cause severe gastrointestinal symptoms.

The actual diagnosis of the presence of an internal biliary fistula

is not of much practical importance, and is rarely made during the clinical examination; it is usually an accidental finding at the operating table. In a few cases the diagnosis has been made preoperatively with the aid of roentgenologic studies. Roentgenographic diagnosis, though rarely applicable, is based upon the demonstration of air or a contrast medium in the biliary passages, thus showing the probable presence of an artificial fistulous tract. One may also suspect the presence of an internal biliary fistula after obtaining a history of symptoms of gallbladder disease, vomiting gallstones or the passage of biliary calculi in the stools.

Treatment

At present the best prophylactic measure is the removal of the gallbladder and of all calculi in the early stages of the biliary tract disease. In the treatment of acute cholecystic disease there are two very definite trends of thought. It is conceded that in many acute abdominal conditions it is safer to operate when the acute symptoms have abated rather than when the attack is at its height. Some very competent surgeons subscribe to this view in dealing with acute cholecystic disease. If "early" operation is interpreted as operation performed within a few hours after the onset of the acute attack, as near as the time of onset can be determined, it will be noted that the tendency is now toward early surgical intervention. The reasons that have been advanced in support of early operation are:

1. The operative procedure is facilitated if the operation takes place before marked evidences of pericholecystic and pericholodochal inflammation have developed;

2. By early operation a possible diagnostic error is obviated; and

3. The incidence and mortality of perforation of the gallbladder with conservative therapy are much higher than heretofore generally believed.[6]

The presence of these communications between the biliary tract and the intestines usually increases the risk of surgical treatment many times over that of uncomplicated biliary tract disease which has an operative mortality of 1 to 5 per cent.[4] A small internal biliary fistula may close spontaneously or cause such mild symptoms that the patient presents himself to the surgeon in good operative condition. On the other hand, a large one is usually so long in healing and so debilitating that operative intervention becomes advisable even though the risk is exceedingly great.

Operations for internal biliary fistulas may be extremely tedious. The surgeon frequently finds the viscera in the right upper abdo-

men to be so closely matted by inflammatory adhesions that no line of cleavage is discernible and adequate exposure is hard to obtain. When the fistula arises from the gallbladder this structure should be removed, whenever local and general conditions permit, and the perforation of the intestines closed. When the duodenum becomes adherent to the gallbladder, or the cystic duct, and a cholecystoduodenal fistula develops, the operation may be exceedingly hard to manage. Difficulty is commonly encountered in separating and closing the duodenum satisfactorily. In some cases it may be advisable to perform a gastroenterostomy to prevent an external duodenal fistula or to overcome any obstruction that may have been caused by closing a large perforation in the duodenum. In the event that an external duodenal fistula does form, a serious postoperative complication is presented. When the lumen is small, the surgeon may excise the fistula and inadvertently overlook the opening in the gut wall, with the result that peritonitis, or a localized abscess, may develop. If the fistulous lumen is large, the cavity must often be drained like any other intra-abdominal abscess.

In view of the high incidence of stones in the hepatic and common ducts in these cases, and the frequently associated infection, exploration and drainage of the ducts will be indicated in many instances. If a fistula is encountered between the common duct and the surrounding viscera, the usual precautions should be taken to prevent a stricture of the duct developing at a later date.

Report of a Case

C. D., a 55 year old white man, was admitted to the hospital complaining of nausea and vomiting. Three months before admission to the hospital he had had a sudden onset of intermittent, colicky pain in the right upper quadrant of his abdomen, followed by nausea and vomiting. Two days later he had become deeply jaundiced and had noticed a tender mass in the region of the gallbladder. The vomitus, at first bile-stained, gradually became fecal in character. Visible jaundice disappeared after a period of 2 weeks, but the tender abdominal mass and frequent fecal vomiting persisted until admission to the hospital. The patient had been unable to retain food taken by mouth and had lost 20 pounds in weight since the onset of symptoms. Previous to the onset of the illness he had not experienced symptoms referable to disease of the biliary or gastro-intestinal tracts.

Physical examination revealed an emaciated, dehydrated white male who appeared chronically ill. Temperature was 37.2°C. There was no clinical evidence of jaundice. There was a large tender mass in the right upper quadrant of the abdomen which varied in size with peristaltic movements of the intestines. The skin over the mass was red and tender. The liver could not be felt. There was referred rebound tenderness to the right upper quadrant of the abdomen, but no evidence of generalized peritonitis.

Accessary clinical findings: Hemoglobin 79 per cent, white blood count 6,100. The urine examination did not reveal any abnormalities. Blood N.P.N.

21 mg. per cent. Fasting Blood sugar 100 mg. per cent. The serum Vanden-Bergh was not elevated. Serum total proteins 4.7 Gm. per cent. A/G ratio 0.42. Roentgenographic examination of the colon following a barium

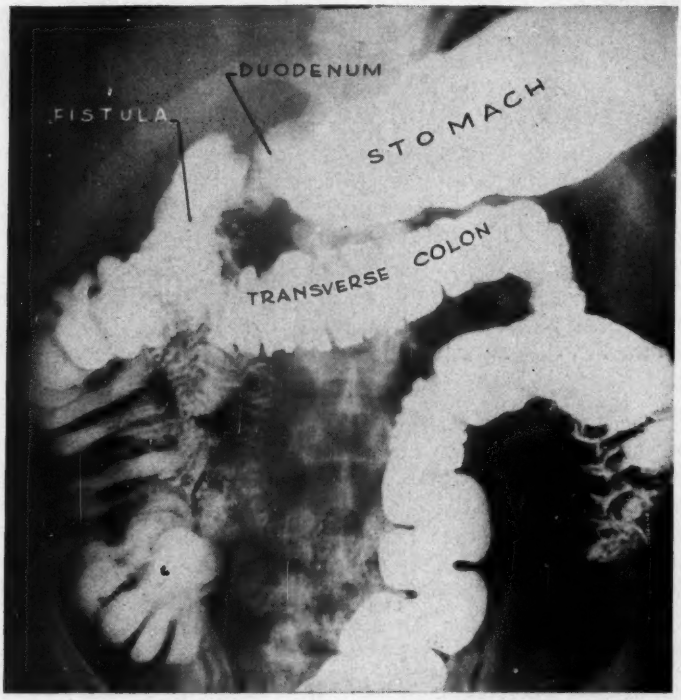

Fig. 1. Roentgenogram, taken after a barium enema had been given, showing a large fistula between the first portion of the duodenum and the proximal portion of the transverse colon.

enema showed good filling as far as the proximal transverse colon. In this region there was a large fistula connecting the colon with the duodenum. The fistulous tract and the stomach were filled with the barium (fig. 1). The diagnosis was internal biliary fistula connecting the gallbladder with the duodenum and colon.

The patient's general condition was poor and extensive preoperative preparation was necessary. To relieve the persistent vomiting, a Levine tube was placed in the stomach and continuous suction applied. Parenteral fluids and several plasma transfusions were administered. Six days after admission to the hospital the patient had a large gastrointestinal hemorrhage, 300 c.c. of blood being aspirated from the stomach through the suction tube. At this time symptoms of pneumonia had appeared and its presence was confirmed by roentgenographic examination. Eighteen hours later another massive gastrointestinal hemorrhage occurred. This resulted in hemorrhagic shock which was controlled with blood transfusions. Due to the recurrent hemorrhages it was thought that operation was advisable at this time, despite the presence of

mild pneumonia. Continuous spinal novocaine was the anesthetic of choice.

At operation a large fistulous tract was found in the subhepatic space extending from the duodenum to the proximal portion of the transverse colon.

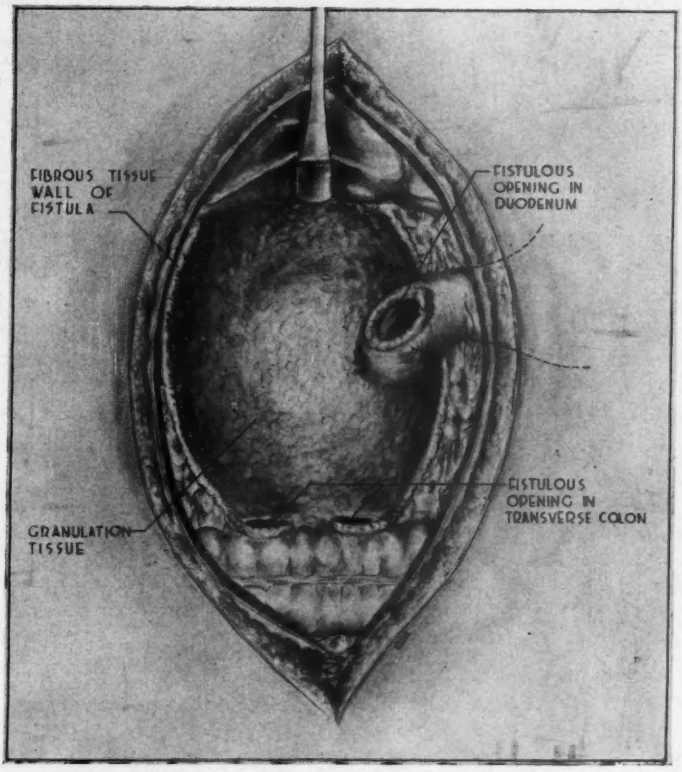
FIBROUS TISSUE WALL OF FISTULA
FISTULOUS OPENING IN DUODENUM
FISTULOUS OPENING IN TRANSVERSE COLON
GRANULATION TISSUE

Fig. 2. Sketch showing the location and relations of the fistulous tract found at the time of the operation. There are two openings in the proximal portion of the transverse colon and one in the first portion of the duodenum.

The fistula was filled with large blood clots and intestinal contents. The wall of the fistulous cavity was composed of omentum and connective tissue and the greater part of this tract was lined with granulation tissue. In some areas the granulation tissue was bleeding; this was thought to be the source of the massive hemorrhages. There were two openings in the proximal portion of the transverse colon and one in the duodenum (fig. 2). The gallbladder had been completely destroyed and the common duct was not identified because of extensive fibrosis in this region. The duodenum and colon appeared normal except for these fistulous openings. There was no scarring or other evidence of previous pathology that could have been the primary cause of the fistula. There was extensive cirrhosis of the liver. The abdominal wall formed the anterior boundary of the fistula and the parietal peritoneum had been destroyed by infection.

The edge of the opening in the duodenum was dissected free with difficulty and after closure of this orifice the lumen was considerably decreased in size. For this reason, and also to prevent an external duodenal fistula, a posterior gastroenterostomy was performed. The fistulous openings in the colon were closed without difficulty. Part of the fistulous tract was excised and the subhepatic space was drained through a stab wound in the right upper quadrant of the abdomen. Biopsy of the fistulous tract did not show any evidence of malignancy. Study of microscopic sections of tissue taken from the wall of the tract revealed extensive fibrosis and a few cells were found which were identical with those of the mucosa of the gallbladder.

The postoperative course was unusually smooth. On the fifth postoperative day the drainage from the stab wound became stained with yellow bile. The bile drainage subsided after a period of 3 weeks, and drainage from the stab wound had completely subsided after 8 weeks. A subcutaneous wound infection occurred which required drainage and secondary closure. The patient was last seen 6 months after operation and at that time he did not have any symptoms referrable to disease of the biliary or gastrointestinal tracts. Fluoroscopy of the stomach revealed the gastroenterostomy to be functioning well, but barium did not pass through the duodenum.

COMMENT

This type of internal biliary fistula is unusual for two reasons: (1) it was connected to the colon and the duodenum, and (2) it was the source of massive hemorrhages. In view of the sudden onset of colicky pain at the beginning of the present illness it is thought that this patient had acute cholecystitis after the cystic duct had become obstructed with a calculus. The fistula probably developed as the result of necrosis of the walls of the gallbladder and intestines. Since the patient's condition was poor, as a result of the massive hemorrhages and prolonged vomiting, he is fortunate to have recovered. The bulk of evidence indicates that most internal fistulas to the gastrointestinal tract can be prevented by early surgical treatment of the predisposing cholecystitis or related biliary tract disease and that the high mortality is a direct result of delay of the patient in coming to operation.

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CAROTID BODY TUMOR

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IN reviewing the literature on carotid body tumors there is a paucity of reference regarding carotid body lesions invading the cranial vault. One case has been reported by H. Rosenwasser[1] in which the process was found in the middle ear and mastoid bone. It is our purpose to present a case of carotid body tumor of the right cervical region with extension into the cranial cavity found on postmortem examination. The autopsy was performed by Dr. M. D. Haley in the Department of Pathology of this institution.

CASE REPORT

The patient was an 80 year old colored male admitted on Nov. 11, 1945, in coma. He died a few hours later and postmortem examination was performed one hour after death.

The history obtained was neither definite nor too reliable. However, it was ascertained that the patient had had a mass in the right neck posterior and inferior to the angle of the mandible for a period of 3 to 4 years. This was accompanied by some drainage from the ear, the character of which is not known. Of interest were seizures of coughing which were accompanied by vomiting. There was an indefinite weight loss. The individual had worked in coal mines for the greater part of his life. There had been no medical care for this tumor.

Physical examination: On admission respirations were labored, with tracheal rattles and wheezes. There was a mass 5 x 7 cm. at the angle of the right mandible from which a draining sinus exuded thick, foul smelling blood and purulent material. Temperature 97°, blood pressure 150/100, respirations 22, labored and shallow. The pupils did not react to light and accommodation. There were loud, coarse and fine rales throughout both lung fields. Cardiac rate was slightly irregular with an occasional ectopic beat, no murmurs. The remainder of the physical examination was negative with the exception of dehydration.

Treatment consisted of the usual supportive measures and the final clinical impression was carcinoma of the mandible.

AUTOPSY FINDINGS

The body is that of an emaciated colored male approximately 80 years of age. The pupils are small, measuring 3 mm. in diameter. There is no jaundice nor edema.

The left ear appears normal. Below the right ear, extending anteriorly and downward, there is a firm mass measuring 4.5 x 4.5 cm. The central portion of said mass is soft with an ulcerated area from which drains a foul smelling,

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sero-sanguinous material. The remainder of the superficial examination is negative.

The peritoneal, pericardial and pleural cavities are not remarkable.

The heart weighs 315 grams. The ascending portion of the aorta is markedly sclerotic, showing numerous elevated yellow plaques. The orifices of the coronary arteries are somewhat narrowed due to the sclerosis. There is an accessory opening for the right coronary artery.

The lungs show some slight nodular consolidation of the left upper lobe.

The spleen and liver show nothing remarkable.

The gastrointestinal tract, pancreas, adrenals and kidneys show no lesions pertinent to the case.

Cranial cavity: The brain weighs 1200 grams. On removing it there is a large amount of slightly cloudy, thin fluid escaping from the anterior portion, apparently from the left lateral ventricle. The brain is very soft and the meninges hyperemic.

At the base of the brain the arteries are rather sclerotic, showing yellow plaques along the whole length. There is a purulent material in the meninges surrounding the base of the brain.

At the right side of the brain stem in the cerebello-medullary-pontine angle there is a rounded mass of rather firm tissue which is pink and somewhat globular. The inferior portion of the right temporal lobe shows a large abscess which is open and draining a thick, yellowish, purulent material.

On sectioning the brain this abscess cavity appears to be connected with the posterior horn of the right lateral ventricle. The ventricular system is dilated and filled with a cloudy, rather thin fluid present within the cavity.

On examining the skull a mass in the right parotid region is seen to extend through the mastoid cells and there is a small abscess in the middle cranial fossa beneath the dura. This is directly beneath the abscess in the brain. Postero-inferior to this, near the opening of the internal auditory meatus there is a polypoid, pedunculated type of growth which is soft and friable. This mass extends through the dura and projects into the middle cranial fossa. Also, there is another small pedunculated type of tumor in the same region which when cut through shows a slight gray, rather firm, homogeneous mass which is well circumscribed. This appears to be a lymph node replaced by tumor tissue. Further anteriorly and medial to the mandible, approximately at the angle, there is another large mass of similar tissue. This piece is light gray, rather firm and more lobulated than the former. This also gives the appearance of a lymph node replaced by tumor tissue.

The right parotid gland is removed together with some of the surrounding tissue. It does not grossly appear to be involved by the above described mass.

Microscopic Interpretation

The sections show a tumor which matches up very well with the appearances of a carotid body tumor as illustrated. In reviewing neoplastic diseases we are listing the tumor as a carotid body tumor. In the region of the carotid the tumor grows with cells which are, for the most part, rather uniform, but in some areas there is a variation in nuclear size. Mitoses are not especially frequent. The tumor cells themselves grow in little bundles and the tumor is quite vascular.

In the cranial cavity the tumor is perhaps better preserved and shows growth of little bundles to better advantage. Study under the high power microscope shows more of the cells having prolongation and composed of parallel fibrillae.

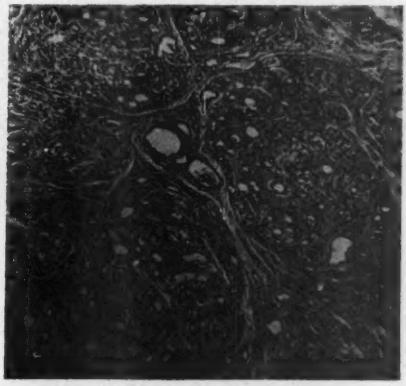

Fig. 1. Normal carotid body

Fig. 2. Tumor

This suggests the possibility that the tumor was derived from the central nervous system.

No definite metastases from the tumor can be demonstrated.

In the adrenal there is hyperplasia of what appears to be nervous tissue, so that there are bundles of fibers sometimes with a palisade arrangement of the nuclei suggesting a neurinoma or Schwannoma. There is a gradation from the neurinoma over into ganglion cells or vice versa. The process is not very large but larger than can be accounted for on the basis of any normal ganglia which were not seen on gross inspection.

Comment

We have presented a rather definite case of carotid body tumor diagnosed from histologic study. However, it must be emphasized that the carotid artery with its bifurcation was not definitely visualized due to restriction at autopsy. Yet, the evidence seems conclusive that this lesion originated within the region of the carotid body and spread superiorly into the cranial vault.

There is abundant literature and references on tumors of the carotid body. These, for the most part, contain a large amount of speculation in regard to the etiologic origin and repetition as to diagnoses and therapy of the carotid body tumors. For the reader's information we have listed a few pertinent references which are current and easily available.

Fig. 3. Site of perforation

In citing this particular case of carotid body tumor it has been of interest in reviewing the literature to ascertain the frequency in which the lesion is seen by a single individual during a lifetime. A consensus is that an active surgeon will see perhaps one and possibly two such lesions during his period of practice. It is most unusual for one to see even three or four such lesions during a lifetime. Hertzler in his publication of "Surgical Pathology of the Diseases of the Neck" states that he has had seven or eight such conditions. This is most remarkable and unusual for no other individual in the literature lists more than four such tumors unless he be connected with a large clinic or institution. Reference is frequently made to an article by Rankin and Wellbrock[4] in which these men report twelve cases of carotid body tumors, one being bilateral.

A conservative estimate of the total number of cases of carotid

body tumors appearing in the literature would be 275. Various figures appear and this is approximately the overall average. Since the publication of Rankin, Harrington, Clagett, and Dockerty[3] have published an article considering 20 tumors of the carotid body. This includes the twelve cases discussed by Rankin and Wellbrock.

The tumors arising from carotid body tissue are, for the most part, hyperplastic in at least 80 to 90 per cent of the cases. Others arising from the nervous tissue or nerve tissue are usually associated with neuroblastomas and neurofibromas. The malignancies include carcinoma, sarcoma and angiosarcoma.

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FUNCTION OF A MEDICAL SCHOOL

The Medical College of Alabama has recently become the seventieth accredited medical school in the United States. It has been created in trying years and in difficult times. Since it is the youngest school in this country, it is but natural that much thought has been given to the basic philosophy of the institution, and this can be expressed in one sentence; namely, to render the greatest service for the public welfare. It is unfortunate that in the past some of our medical schools apparently have not adhered to such a policy with sufficient rigidity. It appears that many of our institutions have become secluded behind ivy-covered walls and have been reluctant to project institutional activities into the fields of public welfare.

A medical school not only conducts an educational program but is also a public service institution. Because of the necessity for offering medical care to thousands of sick people in its teaching program, it is unique in the educational field, as a law school would be if it became necessary to operate the courts to teach young lawyers. It is necessary that the medical school operate large hospitals and project itself into the practical problem of the care of the sick on a mass basis.

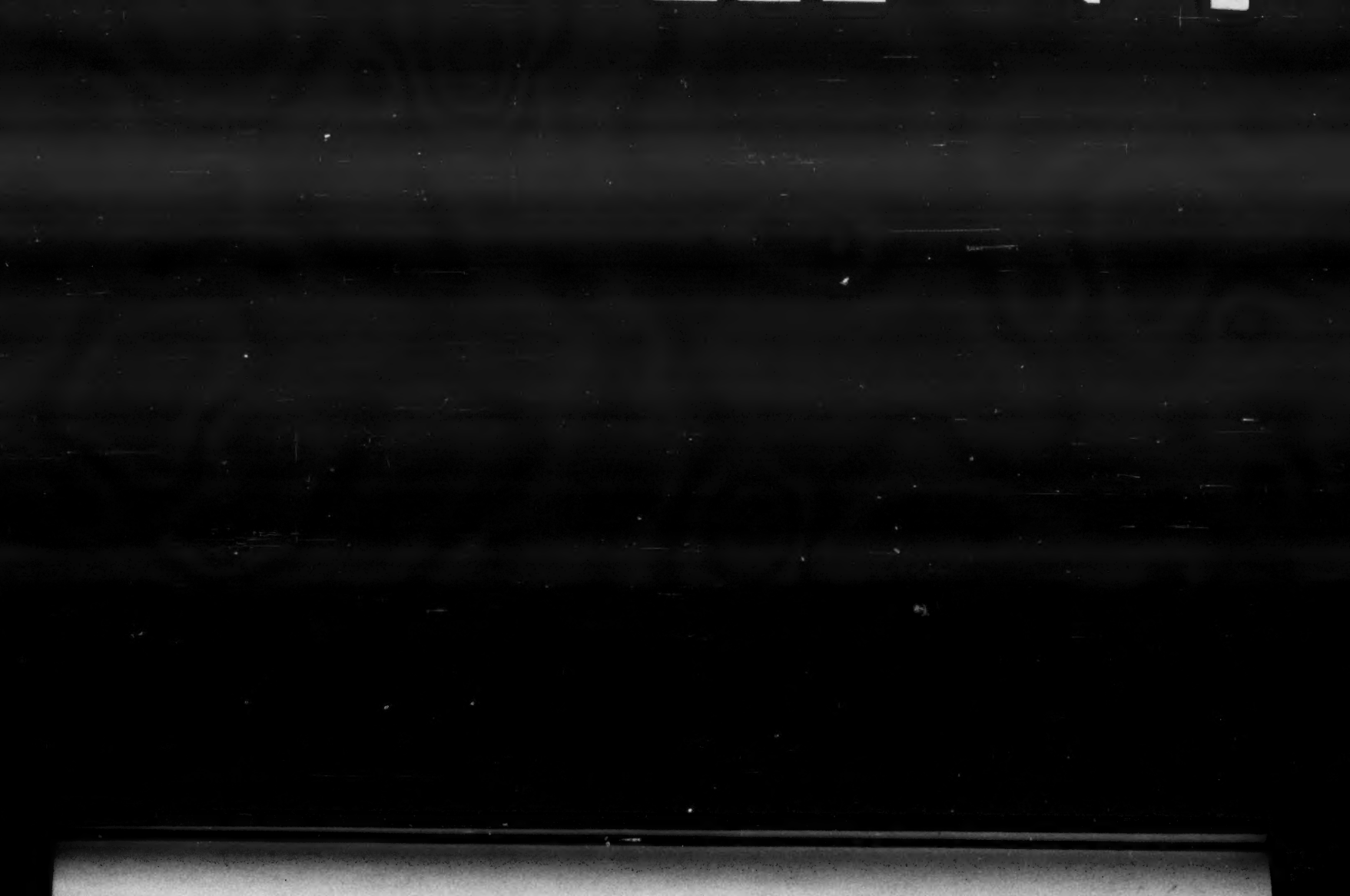
The greater the practical service an institution can render to its country, to its state and to its area the greater is its value to the public which supports it. In this respect there is no difference between state-supported and private institutions since the support

after all comes from a common source and that is the public at large. In one case funds are obtained by taxation and in the other through private philanthropy or other methods. The medical school of the future should concern itself with the practical medical problems of its area and lend its collective brains to their solution. Thus, it should be vitally concerned with such matters as the quality of medical care in its area, with public affairs of all types, and with any and all matters that are pertinent to the public health and public welfare. It should play an active role in guiding the lawmakers in their efforts to improve the public welfare and in every way possible the medical school should make its influence felt for the public good. Only in this way will it be recognized as an instrument for service and develop a social consciousness which the institution may not have if it becomes too secluded in academic isolation.

In the long run such policy will pay great dividends to the school and to medical education, since, after all, the public will support only those agencies of government whose usefulness is daily apparent to the average citizen. Furthermore, if our medical schools and physicians in general give more attention to the economic problems of medical care, we would in the future be better qualified to assume positions of leadership in the formulation of public law relating to medical practice.

The modern medical school should concern itself with the problems of organized medicine and with the problems of medical practice, should lend its efforts to a solution of these problems and should lean heavily on the rank and file of physicians for counsel and advice. It should always keep in the forefront the problems of the general practitioner of medicine.

It is in keeping with such a basic philosophy that this issue of THE SOUTHERN SURGEON is devoted entirely to contributions from members of the Department of Surgery of the Medical College of Alabama and is an illustration of our belief that the modern medical college should work in close harmony with our practicing medical profession.

We are grateful to the editors of THE SOUTHERN SURGEON for opening the pages of this issue to contributions from the Medical College of Alabama.

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